```
                                             1
                                           met ala gln trp glu met leu gln
ACTGCAACCCTAATCAGAGCCCAA                   ATG GCG CAG TGG GAA ATG CTG CAG

     10                                                20
asn leu asp ser pro phe gln asp gln leu his gln leu tyr ser
AAT CTT GAC AGC CCC TTT CAG GAT CAG CTG CAC CAG CTT TAC TCG

                        30
his ser leu leu pro val asp ile arg gln tyr leu ala val trp
CAC AGC CTC CTG CCT GTG GAC ATT CGA CAG TAC TTG GCT GTC TGG

     40                                                50
ile glu asp gln asn trp gln glu ala ala leu gly ser asp asp
ATT GAA GAC CAG AAC TGG CAG GAA GCT GCA CTT GGG AGT GAT GAT

                        60
ser lys ala thr met leu phe phe his phe leu asp gln leu asn
TCC AAG GCT ACC ATG CTA TTC TTC CAC TTC TTG GAT CAG CTG AAC

     70                                                80
tyr glu cys gly arg cys ser gln asp pro glu ser leu leu leu
TAT GAG TGT GGC CGT TGC AGC CAG GAC CCA GAG TCC TTG TTG CTG

                        90
gln his asn leu arg lys phe cys arg asp ile gln pro phe ser
CAG CAC AAT TTG CGG AAA TTC TGC CGG GAC ATT CAG CCC TTT TCC

     100                                               110
gln asp pro thr gln leu ala glu met ile phe asn leu leu leu
CAG GAT CCT ACC CAG TTG GCT GAG ATG ATC TTT AAC CTC CTT CTG

                        120
glu glu lys arg ile leu ile gln ala gln arg ala gln leu glu
GAA GAA AAA AGA ATT TTG ATC CAG GCT CAG AGG GCC CAA TTG GAA

     130                                               140
gln gly glu pro val leu glu thr pro val glu ser gln gln his
CAA GGA GAG CCA GTT CTC GAA ACA CCT GTG GAG AGC CAG CAA CAT

                        150
glu ile glu ser arg ile leu asp leu arg ala met met glu lys
GAG ATT GAA TCC CGG ATC CTG GAT TTA AGG GCT ATG ATG GAG AAG

     160                                               170
leu val lys ser ile ser gln leu lys asp gln gln asp val phe
CTG GTA AAA TCC ATC AGC CAA CTG AAA GAC CAG CAG GAT GTC TTC

                       180
```

Figure 1A

```
cys phe arg tyr lys ile gln ala lys gly lys thr pro ser leu
TGC TTC CGA TAT AAG ATC CAG GCC AAA GGG AAG ACA CCC TCT CTG

    190                                             200
asp pro his gln thr lys glu gln lys ile leu gln glu thr leu
GAC CCC CAT CAG ACC AAA GAG CAG AAG ATT CTG CAG GAA ACT CTC

                        210
asn glu leu asp lys arg arg lys glu val leu asp ala ser lys
AAT GAA CTG GAC AAA AGG AGA AAG GAG GTG CTG GAT GCC TCC AAA

    220                                             230
ala leu leu gly arg leu thr thr leu ile glu leu leu leu pro
GCA CTG CTA GGC CGA TTA ACT ACC CTA ATC GAG CTA CTG CTG CCA

                        240
lys leu glu glu trp lys ala gln gln gln lys ala cys ile arg
AAG TTG GAG GAG TGG AAG GCC CAG CAG CAA AAA GCC TGC ATC AGA

    250                                             260
ala pro ile asp his gly leu glu gln leu glu thr trp phe thr
GCT CCC ATT GAC CAC GGG TTG GAA CAG CTG GAG ACA TGG TTC ACA

                        270
ala gly ala lys leu leu phe his leu arg gln leu leu lys glu
GCT GGA GCA AAG CTG TTG TTT CAC CTG AGG CAG CTG CTG AAG GAG

    280                                             290
leu lys gly leu ser cys leu val ser tyr gln asp asp pro leu
CTG AAG GGA CTG AGT TGC CTG GTT AGC TAT CAG GAT GAC CCT CTG

                        300
thr lys gly val asp leu arg asn ala gln val thr glu leu leu
ACC AAA GGG GTG GAC CTA CGC AAC GCC CAG GTC ACA GAG TTG CTA

    310                                             320
gln arg leu leu his arg ala phe val val glu thr gln pro cys
CAG CGT CTG CTC CAC AGA GCC TTT GTG GTA GAA ACC CAG CCC TGC

                        330
met pro gln thr pro his arg pro leu ile leu lys thr gly ser
ATG CCC CAA ACT CCC CAT CGA CCC CTC ATC CTC AAG ACT GGC AGC

    340                                             350
lys phe thr val arg thr arg leu leu val arg leu gln glu gly
AAG TTC ACC GTC CGA ACA AGG CTG CTG GTG AGA CTC CAG GAA GGC

                        360
asn glu ser leu thr val glu val ser ile asp arg asn pro pro
AAT GAG TCA CTG ACT GTG GAA GTC TCC ATT GAC AGG AAT CCT CCT

    370                                             380
gln leu gln gly phe arg lys phe asn ile leu thr ser asn gln
CAA TTA CAA GGC TTC CGG AAG TTC AAC ATT CTG ACT TCA AAC CAG

                        390
lys thr leu thr pro glu lys gly gln ser gln gly leu ile trp
```

Figure 1B

```
AAA ACT TTG ACC CCC GAG AAG GGG CAG AGT CAG GGT TTG ATT TGG

    400                                                 410
asp phe gly tyr leu thr leu val glu gln arg ser gly gly ser
GAC TTT GGT TAC CTG ACT CTG GTG GAG CAA CGT TCA GGT GGT TCA

                        420
gly lys gly ser asn lys gly pro leu gly val thr glu glu leu
GGA AAG GGC AGC AAT AAG GGG CCA CTA GGT GTG ACA GAG GAA CTG

    430                                                 440
his ile ile ser phe thr val lys tyr thr tyr gln gly leu lys
CAC ATC ATC AGC TTC ACG GTC AAA TAT ACC TAC CAG GGT CTG AAG

                        450
gln glu leu lys thr asp thr leu pro val val ile ile ser asn
CAG GAG CTG AAA ACG GAC ACC CTC CCT GTG GTG ATT ATT TCC AAC

    460                                                 470
met asn gln leu ser ile ala trp ala ser val leu trp phe asn
ATG AAC CAG CTC TCA ATT GCC TGG GCT TCA GTT CTC TGG TTC AAT

                        480
leu leu ser pro asn leu gln asn gln gln phe phe ser asn pro
TTG CTC AGC CCA AAC CTT CAG AAC CAG CAG TTC TTC TCC AAC CCC

    490                                                 500
pro lys ala pro trp ser leu leu gly pro ala leu ser trp gln
CCC AAG GCC CCC TGG AGC TTG CTG GGC CCT GCT CTC AGT TGG CAG

                        510
phe ser ser tyr val gly arg gly leu asn ser asp gln leu ser
TTC TCC TCC TAT GTT GGC CGA GGC CTC AAC TCA GAC CAG CTG AGC

    520                                                 530
met leu arg asn lys leu phe gly gln asn cys arg thr glu asp
ATG CTG AGA AAC AAG CTG TTC GGG CAG AAC TGT AGG ACT GAG GAT

                        540
pro leu leu ser trp ala asp phe thr lys arg glu ser pro pro
CCA TTA TTG TCC TGG GCT GAC TTC ACT AAG CGA GAG AGC CCT CCT

    550                                                 560
gly lys leu pro phe trp thr trp leu asp lys ile leu glu leu
GGC AAG TTA CCA TTC TGG ACA TGG CTG GAC AAA ATT CTG GAG TTG

                        570
val his asp his leu lys asp leu trp asn asp gly arg ile met
GTA CAT GAC CAC CTG AAG GAT CTC TGG AAT GAT GGA CGC ATC ATG

    580                                                 590
gly phe val ser arg ser gln glu arg arg leu leu lys lys thr
GGC TTT GTG AGT CGG AGC CAG GAG CGC CGG CTG CTG AAG AAG ACC

                        600
met ser gly thr phe leu leu arg phe ser glu ser ser glu gly
ATG TCT GGC ACC TTT CTA CTG CGC TTC AGT GAA TCG TCA GAA GGG
```

Figure 1C

```
    610                                                 620
gly ile thr cys ser trp val glu his gln asp asp asp lys val
GGC ATT ACC TGC TCC TGG GTG GAG CAC CAG GAT GAT GAC AAG GTG

                        630
leu ile tyr ser val gln pro tyr thr lys glu val leu gln ser
CTC ATC TAC TCT GTG CAA CCG TAC ACG AAG GAG GTG CTG CAG TCA

    640                                                 650
leu pro leu thr glu ile ile arg his tyr gln leu leu thr glu
CTC CCG CTG ACT GAA ATC ATC CGC CAT TAC CAG TTG CTC ACT GAG

                        660
glu asn ile pro glu asn pro leu arg phe leu tyr pro arg ile
GAG AAT ATA CCT GAA AAC CCA CTG CGC TTC CTC TAT CCC CGA ATC

    670                                                 680
pro arg asp glu ala phe gly cys tyr tyr gln glu lys val asn
CCC CGG GAT GAA GCT TTT GGG TGC TAC TAC CAG GAG AAA GTT AAT

                        690
leu gln glu arg arg lys tyr leu lys his arg leu ile val val
CTC CAG GAA CGG AGG AAA TAC CTG AAA CAC AGG CTC ATT GTG GTC

    700                                                 710
ser asn arg gln val asp glu leu gln gln pro leu glu leu lys
TCT AAT AGA CAG GTG GAT GAA CTG CAA CAA CCG CTG GAG CTT AAG

                        720
pro glu pro glu leu glu ser leu glu leu glu leu gly leu val
CCA GAG CCA GAG CTG GAG TCA TTA GAG CTG GAA CTA GGG CTG GTG

    730                                                 740
pro glu pro glu leu ser leu asp leu glu pro leu leu lys ala
CCA GAG CCA GAG CTC AGC CTG GAC TTA GAG CCA CTG CTG AAG GCA

                        750
gly leu asp leu gly pro glu leu glu ser val leu glu ser thr
GGG CTG GAT CTG GGG CCA GAG CTA GAG TCT GTG CTG GAG TCC ACT

    760                                                 770
leu glu pro val ile glu pro thr leu cys met val ser gln thr
CTG GAG CCT GTG ATA GAG CCC ACA CTA TGC ATG GTA TCA CAA ACA

                        780
val pro glu pro asp gln gly pro val ser gln pro val pro glu
GTG CCA GAG CCA GAC CAA GGA CCT GTA TCA CAG CCA GTG CCA GAG

    790                                                 800
pro asp leu pro cys asp leu arg his leu asn thr glu pro met
CCA GAT TTG CCC TGT GAT CTG AGA CAT TTG AAC ACT GAG CCA ATG

                        810
glu ile phe arg asn cys val lys ile glu glu ile met pro asn
GAA ATC TTC AGA AAC TGT GTA AAG ATT GAA GAA ATC ATG CCG AAT
```

Figure 1D

```
    020                                                 030
gly asp pro leu leu ala gly gln asn thr val asp glu val tyr
GGT GAC CCA CTG TTG GCT GGC CAG AAC ACC GTG GAT GAG GTT TAC

                        040
val ser arg pro ser his phe tyr thr asp gly pro leu met pro
GTC TCC CGC CCC AGC CAC TTC TAC ACT GAT GGA CCC TTG ATG CCT

    050 051
ser asp phe AM
TCT GAC TTC TAG GAACCACATTTCCTCTGTTCTTTTCATATCTCTTTGCCCTTCCTA

CTCCTCATAGCATGATATTGTTCTCCAAGGATGGGAATCAGGCATGTGTCCCTTCCAAGC

TGTGTTAACTGTTCAAACTCAGGCCTGTGTGACTCCATTGGGGTGAGAGGTGAAAGCATA

ACATGGGTACAGAGGGGACAACAATGAATCAGAACAGATGCTGAGCCATAGGTCTAAATA

GGATCCTGGAGGCTGCCTGCTGTGCTGGGAGGTATAGGGGTCCTGGGGGCAGGCCAGGGC

AGTTGACAGGTACTTGGAGGGCTCAGGGCAGTGGCTTCTTTCCAGTATGGAAGGATTTCA

ACATTTTAATAGTTGGTTAGGCTAAACTGGTGCATACTGGCATTGGCCTTGGTGGGGAGC

ACAGACACAGGATAGGACTCCATTTCTTTCTTCCATTCCTTCATGTCTAGGATAACTTGC

TTTCTTCTTTCCTTTACTCCTGGCTCAAGCCCTGAATTTCTTCTTTTCCTGCAGGGTTG

AGAGCTTTCTGCCTTAGCCTACCATGTGAAACTCTACCCTGAAGAAAGGGATGGATAGGA

AGTAGACCTCTTTTTCTTACCAGTCTCCTCCCCTACTCTGCCCCCTAAGCTGGCTGTACC

TGTTCCTCCCCCATAAAAATGATCCTGCCAATCTAAAAAAAAAA
```

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Figure 1E

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ATTAAACCTCTCGGCGAGCCCCTCCGCAGACTCTGCGCCGGAAAGTTTCATTTGCTGTATGCCATCCTCGA

GAGCTGTCTAGGTTAACGTTCGCACTCTGTGTATATAACCTCGACAGTCTTGGCACCTAACGTGCTGTGCG

                                                          Met Ser Gln Trp
TAGCTGCTCCTTTGGTTGAATCCCCAGGCCCTTGTTGGGGCACAAGGTGGCAGG ATG TCT CAG TGG

Tyr Glu Leu Gln Gln Leu Asp Ser Lys Phe Leu Glu Gln Val His Gln Leu Tyr
TAC GAA CTT CAG CAG CTT GAC TCA AAA TTC CTG GAG CAG GTT CAC CAG CTT TAT

Asp Asp Ser Phe Pro Met Glu Ile Arg Gln Tyr Leu Ala Gln Trp Leu Glu Lys
GAT GAC AGT TTT CCC ATG GAA ATC AGA CAG TAC CTG GCA CAG TGG TTA GAA AAG

Gln Asp Trp Glu His Ala Ala Asn Asp Val Ser Phe Ala Thr Ile Arg Phe His
CAA GAC TGG GAG CAC GCT GCC AAT GAT GTT TCA TTT GCC ACC ATC CGT TTT CAT

Asp Leu Leu Ser Gln Leu Asp Asp Gln Tyr Ser Arg Phe Ser Leu Glu Asn Asn
GAC CTC CTG TCA CAG CTG GAT GAT CAA TAT AGT CGC TTT TCT TTG GAG AAT AAC

Phe Leu Leu Gln His Asn Ile Arg Lys Ser Lys Arg Asn Leu Gln Asp Asn Phe
TTC TTG CTA CAG CAT AAC ATA AGG AAA AGC AAG CGT AAT CTT CAG GAT AAT TTT

Gln Glu Asp Pro Ile Gln Met Ser Met Ile Ile Tyr Ser Cys Leu Lys Glu Glu
CAG GAA GAC CCA ATC CAG ATG TCT ATG ATC ATT TAC AGC TGT CTG AAG GAA GAA

Arg Lys Ile Leu Glu Asn Ala Gln Arg Phe Asn Gln Ala Gln Ser Gly Asn Ile
AGG AAA ATT CTG GAA AAC GCC CAG AGA TTT AAT CAG GCT CAG TCG GGG AAT ATT

Gln Ser Thr Val Met Leu Asp Lys Gln Lys Glu Leu Asp Ser Lys Val Arg Asn
CAG AGC ACA GTG ATG TTA GAC AAA CAG AAA GAG CTT GAC AGT AAA GTC AGA AAT

Val Lys Asp Lys Val Met Cys Ile Glu His Glu Ile Lys Ser Leu Glu Asp Leu
GTG AAG GAC AAG GTT ATG TGT ATA GAG CAT GAA ATC AAG AGC CTG GAA GAT TTA

Gln Asp Glu Tyr Asp Phe Lys Cys Lys Thr Leu Gln Asn Arg Glu His Glu Thr
CAA GAT GAA TAT GAC TTC AAA TGC AAA ACC TTG CAG AAC AGA GAA CAC GAG ACC

Asn Gly Val Ala Lys Ser Asp Gln Lys Gln Glu Gln Leu Leu Leu Lys Lys Met
AAT GGT GTG GCA AAG AGT GAT CAG AAA CAA GAA CAG CTG TTA CTC AAG AAG ATG

Tyr Leu Met Leu Asp Asn Lys Arg Lys Glu Val Val His Lys Ile Ile Glu Leu
TAT TTA ATG CTT GAC AAT AAG AGA AAG GAA GTA GTT CAC AAA ATA ATA GAG TTG

Leu Asn Val Thr Glu Leu Thr Gln Asn Ala Leu Ile Asn Asp Glu Leu Val Glu
CTG AAT GTC ACT GAA CTT ACC CAG AAT GCC CTG ATT AAT GAT GAA CTA GTG GAG

Trp Lys Arg Arg Gln Gln Ser Ala Cys Ile Gly Gly Pro Pro Asn Ala Cys Leu
TGG AAG CGG AGA CAG CAG AGC GCC TGT ATT GGG GGG CCG CCC AAT GCT TGC TTG

Asp Gln Leu Gln Asn Trp Phe Thr Ile Val Ala Glu Ser Leu Gln Gln Val Arg
GAT CAG CTG CAG AAC TGG TTC ACT ATA GTT GCG GAG AGT CTG CAG CAA GTT CGG

Gln Gln Leu Lys Lys Leu Glu Glu Leu Glu Gln Lys Tyr Thr Tyr Glu His Asp
CAG CAG CTT AAA AAG TTG GAG GAA TTG GAA CAG AAA TAC ACC TAC GAA CAT GAC

Pro Ile Thr Lys Asn Lys Gln Val Leu Trp Asp Arg Thr Phe Ser Leu Phe Gln
CCT ATC ACA AAA AAC AAA CAA GTG TTA TGG GAC CGC ACC TTC AGT CTT TTC CAG
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Figure 2A

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Gln Leu Ile Gln Ser Ser Phe Val Val Glu Arg Gln Pro Cys Met Pro Thr His
CAG CTC ATT CAG AGC TCG TTT GTG GTG GAA AGA CAG CCC TGC ATG CCA ACG CAC

Pro Gln Arg Pro Leu Val Leu Lys Thr Gly Val Gln Phe Thr Val Lys Leu Arg
CCT CAG AGG CCG CTG GTC TTG AAG ACA GGG GTC CAG TTC ACT GTG AAG TTG AGA

Leu Leu Val Lys Leu Gln Glu Leu Asn Tyr Asn Leu Lys Val Lys Val Leu Phe
CTG TTG GTG AAA TTG CAA GAG CTG AAT TAT AAT TTG AAA GTC AAA GTC TTA TTT

Asp Lys Asp Val Asn Glu Arg Asn Thr Val Lys Gly Phe Arg Lys Phe Asn Ile
GAT AAA GAT GTG AAT GAG AGA AAT ACA GTA AAA GGA TTT AGG AAG TTC AAC ATT

Leu Gly Thr His Thr Lys Val Met Asn Met Glu Glu Ser Thr Asn Gly Ser Leu
TTG GGC ACG CAC ACA AAA GTG ATG AAC ATG GAG GAG TCC ACC AAT GGC AGT CTG

Ala Ala Glu Phe Arg His Leu Gln Leu Lys Glu Gln Lys Asn Ala Gly Thr Arg
GCG GCT GAA TTT CGG CAC CTG CAA TTG AAA GAA CAG AAA AAT GCT GGC ACC AGA

Thr Asn Glu Gly Pro Leu Ile Val Thr Glu Glu Leu His Ser Leu Ser Phe Glu
ACG AAT GAG GGT CCT CTC ATC GTT ACT GAA GAG CTT CAC TCC CTT AGT TTT GAA

Thr Gln Leu Cys Gln Pro Gly Leu Val Ile Asp Leu Glu Thr Thr Ser Leu Pro
ACC CAA TTG TGC CAG CCT GGT TTG GTA ATT GAC CTC GAG ACG ACC TCT CTG CCC

Val Val Val Ile Ser Asn Val Ser Gln Leu Pro Ser Gly Trp Ala Ser Ile Leu
GTT GTG GTG ATC TCC AAC GTC AGC CAG CTC CCG AGC GGT TGG GCC TCC ATC CTT

Trp Tyr Asn Met Leu Val Ala Glu Pro Arg Asn Leu Ser Phe Phe Leu Thr Pro
TGG TAC AAC ATG CTG GTG GCG GAA CCC AGG AAT CTG TCC TTC TTC CTG ACT CCA

Pro Cys Ala Arg Trp Ala Gln Leu Ser Glu Val Leu Ser Trp Gln Phe Ser Ser
CCA TGT GCA CGA TGG GCT CAG CTT TCA GAA GTG CTG AGT TGG CAG TTT TCT TCT

Val Thr Lys Arg Gly Leu Asn Val Asp Gln Leu Asn Met Leu Gly Glu Lys Leu
GTC ACC AAA AGA GGT CTC AAT GTG GAC CAG CTG AAC ATG TTG GGA GAG AAG CTT

Leu Gly Pro Asn Ala Ser Pro Asp Gly Leu Ile Pro Trp Thr Arg Phe Cys Lys
CTT GGT CCT AAC GCC AGC CCC GAT GGT CTC ATT CCG TGG ACG AGG TTT TGT AAG

Glu Asn Ile Asn Asp Lys Asn Phe Pro Phe Trp Leu Trp Ile Glu Ser Ile Leu
GAA AAT ATA AAT GAT AAA AAT TTT CCC TTC TGG CTT TGG ATT GAA AGC ATC CTA

Glu Leu Ile Lys Lys His Leu Leu Pro Leu Trp Asn Asp Gly Cys Ile Met Gly
GAA CTC ATT AAA AAA CAC CTG CTC CCT CTC TGG AAT GAT GGG TGC ATC ATG GGC

Phe Ile Ser Lys Glu Arg Glu Arg Ala Leu Leu Lys Asp Gln Gln Pro Gly Thr
TTC ATC AGC AAG GAG CGA GAG CGT GCC CTG TTG AAG GAC CAG CAG CCG GGG ACC

Phe Leu Leu Arg Phe Ser Glu Ser Ser Arg Glu Gly Ala Ile Thr Phe Thr Trp
TTC CTG CTG CGG TTC AGT GAG AGC TCC CGG GAA GGG GCC ATC ACA TTC ACA TGG

Val Glu Arg Ser Gln Asn Gly Gly Glu Pro Asp Phe His Ala Val Glu Pro Tyr
GTG GAG CGG TCC CAG AAC GGA GGC GAA CCT GAC TTC CAT GCG GTT GAA CCC TAC

Thr Lys Lys Glu Leu Ser Ala Val Thr Phe Pro Asp Ile Ile Arg Asn Tyr Lys
ACG AAG AAA GAA CTT TCT GCT GTT ACT TTC CCT GAC ATC ATT CGC AAT TAC AAA

Val Met Ala Ala Glu Asn Ile Pro Glu Asn Pro Leu Lys Tyr Leu Tyr Pro Asn
GTC ATG GCT GCT GAG AAT ATT CCT GAG AAT CCC CTG AAG TAT CTG TAT CCA AAT
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Figure 2B

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Ile Asp Lys Asp His Ala Phe Gly Lys Tyr Tyr Ser Arg Pro Lys Glu Ala Pro
ATT GAC AAA GAC CAT GCC TTT GGA AAG TAT TAC TCC AGG CCA AAG GAA GCA CCA

Glu Pro Met Glu Leu Asp Gly Pro Lys Gly Thr Gly Tyr Ile Lys Thr Glu Leu
GAG CCA ATG GAA CTT GAT GGC CCT AAA GGA ACT GGA TAT ATC AAG ACT GAG TTG

Ile Ser Val Ser Glu Val His Pro Ser Arg Leu Gln Thr Thr Asp Asn Leu Leu
ATT TCT GTG TCT GAA GTT CAC CCT TCT AGA CTT CAG ACC ACA GAC AAC CTG CTC

Pro Met Ser Pro Glu Glu Phe Asp Glu Val Ser Arg Ile Val Gly Ser Val Glu
CCC ATG TCT CCT GAG GAG TTT GAC GAG GTG TCT CGG ATA GTG GGC TCT GTA GAA

Phe Asp Ser Met Met Asn Thr Val
TTC GAC AGT ATG ATG AAC ACA GTA TAGAGCATGAATTTTTTTCATCTTCTCTGGCGACAGTTT

TCCTTCTCATCTGTGATTCCCTCCTGCTACTCTGTTCCTTCACATCCTGTGTTTCTAGGGAAATGAAAGAA

AGGCCAGCAAATTCGCTGCAACCTGTTGATAGCAAGTGAATTTTTCTCTAACTCAGAAACATCAGTTACTC

TGAAGGGCATCATGCATCTTACTGAAGGTAAAATTGAAAGGCATTCTCTGAAGAGTGGGTTTCACAAGTGA

AAAACATCCAGATACACCCAAAGTATCAGGACGAGAATGAGGGTCCTTTGGGAAAGGAGAAGTTAAGCAAC

ATCTAGCAAATGTTATGCATAAAGTCAGTGCCCAACTGTTATAGGTTGTTGGATAAATCAGTGGTTATTTA

GGGAACTGCTTGACGTAGGAACGGTAAATTTCTGTGGGAGAATTCTTACATGTTTTCTTTGCTTTAAGTGT

AACTGGCAGTTTTCCATTGGTTTACCTGTGAAATAGTTCAAAGCCAAGTTTATATACAATTATATCAGTCC

TCTTTCAAAGGTAGCCATCATGGATCTGGTAGGGGGAAAATGTGTATTTTATTACATCTTTCACATTGGCT

ATTTAAAGACAAAGACAAATTCTGTTTCTTGAGAAGAGAATATTAGCTTTACTGTTTGTTATGGCTTAATG

ACACTAGCTAATATCAATAGAAGGATGTACATTTCCAAATTCACAAGTTGTGTTTGATATCCAAAGCTGAA

TACATTCTGCTTTCATCTTGGTCACATACAATTATTTTTACAGTTCTCCCAAGGGAGTTAGGCTATTCACA

ACCACTCATTCAAAAGTTGAAATTAACCATAGATGTAGATAAACTCAGAAATTTAATTCATGTTTCTTAAA

TGGGCTACTTTGTCCTTTTTGTTATTAGGGTGGTATTTAGTCTATTAGCCACAAAATTGGGAAAGGAGTAG

AAAAAGCAGTAACTGACAACTTGAATAATACACCAGAGATAATATGAGAATCAGATCATTTCAAAACTCAT

TTCCTATGTAACTGCATTGAGAACTGCATATGTTTCGCTGATATATGTGTTTTTCACATTTGCGAATGGTT
```

Figure 2C

CCATTCTCTCTCCTGTACTTTTTCCAGACACTTTTTTGAGTGGATGATGTTTCGTGAAGTATACTGTATTT

TTACCTTTTTCCTTCCTTATCACTGACACAAAAAGTAGATTAAGAGATGGGTTTGACAAGGTTCTTCCCTT

TTACATACTGCTGTCTATGTGGCTGTATCTTGTTTTTCCACTACTGCTACCACAACTATATTATCATGCAA

ATGCTGTATTCTTCTTTGGTGGAGATAAAGATTTCTTGAGTTTTGTTTTAAAATTAAAGCTAAAGTATCTG

TATTGCATTAAATATAATATCGACACAGTGCTTTCCGTGGCACTGCATACAATCTGAGGCCTCCTCTCTCA

GTTTTTATATAGATGGCGAGAACCTAAGTTTCAGTTGATTTTACAATTGAAATGACTAAAAAACAAAGAAG

ACAACATTAAAAACAATATTGTTTCTA

Figure 2D

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ATTAAACCTCTCGCCGAGCCCCTCCGCAGACTCTGCGCCGGAAAGTTTCATTTGCTGTATGCCATCCTCGA

GAGCTGTCTAGGTTAACGTTCGCACTCTGTGTATATAACCTCGACAGTCTTGGCACCTAACGTGCTGTGCG

                                                                Met Ser Gln Trp
TAGCTGCTCCTTTGGTTGAATCCCCAGGCCCTTGTTGGGGCACAAGGTGGCAGG ATG TCT CAG TGG

Tyr Glu Leu Gln Gln Leu Asp Ser Lys Phe Leu Glu Gln Val His Gln Leu Tyr
TAC GAA CTT CAG CAG CTT GAC TCA AAA TTC CTG GAG CAG GTT CAC CAG CTT TAT

Asp Asp Ser Phe Pro Met Glu Ile Arg Gln Tyr Leu Ala Gln Trp Leu Glu Lys
GAT GAC AGT TTT CCC ATG GAA ATC AGA CAG TAC CTG GCA CAG TGG TTA GAA AAG

Gln Asp Trp Glu His Ala Ala Asn Asp Val Ser Phe Ala Thr Ile Arg Phe His
CAA GAC TGG GAG CAC GCT GCC AAT GAT GTT TCA TTT GCC ACC ATC CGT TTT CAT

Asp Leu Leu Ser Gln Leu Asp Asp Gln Tyr Ser Arg Phe Ser Leu Glu Asn Asn
GAC CTC CTG TCA CAG CTG GAT GAT CAA TAT AGT CGC TTT TCT TTG GAG AAT AAC

Phe Leu Leu Gln His Asn Ile Arg Lys Ser Lys Arg Asn Leu Gln Asp Asn Phe
TTC TTG CTA CAG CAT AAC ATA AGG AAA AGC AAG CGT AAT CTT CAG GAT AAT TTT

Gln Glu Asp Pro Ile Gln Met Ser Met Ile Ile Tyr Ser Cys Leu Lys Glu Glu
CAG GAA GAC CCA ATC CAG ATG TCT ATG ATC ATT TAC AGC TGT CTG AAG GAA GAA

Arg Lys Ile Leu Glu Asn Ala Gln Arg Phe Asn Gln Ala Gln Ser Gly Asn Ile
AGG AAA ATT CTG GAA AAC GCC CAG AGA TTT AAT CAG GCT CAG TCG GGG AAT ATT

Gln Ser Thr Val Met Leu Asp Lys Gln Lys Glu Leu Asp Ser Lys Val Arg Asn
CAG AGC ACA GTG ATG TTA GAC AAA CAG AAA GAG CTT GAC AGT AAA GTC AGA AAT

Val Lys Asp Lys Val Met Cys Ile Glu His Glu Ile Lys Ser Leu Glu Asp Leu
GTG AAG GAC AAG GTT ATG TGT ATA GAG CAT GAA ATC AAG AGC CTG GAA GAT TTA

Gln Asp Glu Tyr Asp Phe Lys Cys Lys Thr Leu Gln Asn Arg Glu His Glu Thr
CAA GAT GAA TAT GAC TTC AAA TGC AAA ACC TTG CAG AAC AGA GAA CAC GAG ACC

Asn Gly Val Ala Lys Ser Asp Gln Lys Gln Glu Gln Leu Leu Leu Lys Lys Met
AAT GGT GTG GCA AAG AGT GAT CAG AAA CAA GAA CAG CTG TTA CTC AAG AAG ATG

Tyr Leu Met Leu Asp Asn Lys Arg Lys Glu Val Val His Lys Ile Ile Glu Leu
TAT TTA ATG CTT GAC AAT AAG AGA AAG GAA GTA GTT CAC AAA ATA ATA GAG TTG

Leu Asn Val Thr Glu Leu Thr Gln Asn Ala Leu Ile Asn Asp Glu Leu Val Glu
CTG AAT GTC ACT GAA CTT ACC CAG AAT GCC CTG ATT AAT GAT GAA CTA GTG GAG

Trp Lys Arg Arg Gln Gln Ser Ala Cys Ile Gly Gly Pro Pro Asn Ala Cys Leu
TGG AAG CGG AGA CAG CAG AGC GCC TGT ATT GGG GGG CCG CCC AAT GCT TGC TTG

Asp Gln Leu Gln Asn Trp Phe Thr Ile Val Ala Glu Ser Leu Gln Gln Val Arg
GAT CAG CTG CAG AAC TGG TTC ACT ATA GTT GCG GAG AGT CTG CAG CAA GTT CGG

Gln Gln Leu Lys Lys Leu Glu Glu Leu Glu Gln Lys Tyr Thr Tyr Glu His Asp
CAG CAG CTT AAA AAG TTG GAG GAA TTG GAA CAG AAA TAC ACC TAC GAA CAT GAC

Pro Ile Thr Lys Asn Lys Gln Val Leu Trp Asp Arg Thr Phe Ser Leu Phe Gln
CCT ATC ACA AAA AAC AAA CAA GTG TTA TGG GAC CGC ACC TTC AGT CTT TTC CAG
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Figure 3A

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Gln Leu Ile Gln Ser Ser Phe Val Val Glu Arg Gln Pro Cys Met Pro Thr His
CAG CTC ATT CAG AGC TCG TTT GTG GTG GAA AGA CAG CCC TGC ATG CCA ACG CAC

Pro Gln Arg Pro Leu Val Leu Lys Thr Gly Val Gln Phe Thr Val Lys Leu Arg
CCT CAG AGG CCG CTG GTC TTG AAG ACA GGG GTC CAG TTC ACT GTG AAG TTG AGA

Leu Leu Val Lys Leu Gln Glu Leu Asn Tyr Asn Leu Lys Val Lys Val Leu Phe
CTG TTG GTG AAA TTG CAA GAG CTG AAT TAT AAT TTG AAA GTC AAA GTC TTA TTT

Asp Lys Asp Val Asn Glu Arg Asn Thr Val Lys Gly Phe Arg Lys Phe Asn Ile
GAT AAA GAT GTG AAT GAG AGA AAT ACA GTA AAA GGA TTT AGG AAG TTC AAC ATT

Leu Gly Thr His Thr Lys Val Met Asn Met Glu Glu Ser Thr Asn Gly Ser Leu
TTG GGC ACG CAC ACA AAA GTG ATG AAC ATG GAG GAG TCC ACC AAT GGC AGT CTG

Ala Ala Glu Phe Arg His Leu Gln Leu Lys Glu Gln Lys Asn Ala Gly Thr Arg
GCG GCT GAA TTT CGG CAC CTG CAA TTG AAA GAA CAG AAA AAT GCT GGC ACC AGA

Thr Asn Glu Gly Pro Leu Ile Val Thr Glu Glu Leu His Ser Leu Ser Phe Glu
ACG AAT GAG GGT CCT CTC ATC GTT ACT GAA GAG CTT CAC TCC CTT AGT TTT GAA

Thr Gln Leu Cys Gln Pro Gly Leu Val Ile Asp Leu Glu Thr Thr Ser Leu Pro
ACC CAA TTG TGC CAG CCT GGT TTG GTA ATT GAC CTC GAG ACG ACC TCT CTG CCC

Val Val Val Ile Ser Asn Val Ser Gln Leu Pro Ser Gly Trp Ala Ser Ile Leu
GTT GTG GTG ATC TCC AAC GTC AGC CAG CTC CCG AGC GGT TGG GCC TCC ATC CTT

Trp Tyr Asn Met Leu Val Ala Glu Pro Arg Asn Leu Ser Phe Phe Leu Thr Pro
TGG TAC AAC ATG CTG GTG GCG GAA CCC AGG AAT CTG TCC TTC TTC CTG ACT CCA

Pro Cys Ala Arg Trp Ala Gln Leu Ser Glu Val Leu Ser Trp Gln Phe Ser Ser
CCA TGT GCA CGA TGG GCT CAG CTT TCA GAA GTG CTG AGT TGG CAG TTT TCT TCT

Val Thr Lys Arg Gly Leu Asn Val Asp Gln Leu Asn Met Leu Gly Glu Lys Leu
GTC ACC AAA AGA GGT CTC AAT GTG GAC CAG CTG AAC ATG TTG GGA GAG AAG CTT

Leu Gly Pro Asn Ala Ser Pro Asp Gly Leu Ile Pro Trp Thr Arg Phe Cys Lys
CTT GGT CCT AAC GCC AGC CCC GAT GGT CTC ATT CCG TGG ACG AGG TTT TGT AAG

Glu Asn Ile Asn Asp Lys Asn Phe Pro Phe Trp Leu Trp Ile Glu Ser Ile Leu
GAA AAT ATA AAT GAT AAA AAT TTT CCC TTC TGG CTT TGG ATT GAA AGC ATC CTA

Glu Leu Ile Lys Lys His Leu Leu Pro Leu Trp Asn Asp Gly Cys Ile Met Gly
GAA CTC ATT AAA AAA CAC CTG CTC CCT CTC TGG AAT GAT GGG TGC ATC ATG GGC

Phe Ile Ser Lys Glu Arg Glu Arg Ala Leu Leu Lys Asp Gln Gln Pro Gly Thr
TTC ATC AGC AAG GAG CGA GAG CGT GCC CTG TTG AAG GAC CAG CAG CCG GGG ACC

Phe Leu Leu Arg Phe Ser Glu Ser Ser Arg Glu Gly Ala Ile Thr Phe Thr Trp
TTC CTG CTG CGG TTC AGT GAG AGC TCC CGG GAA GGG GCC ATC ACA TTC ACA TGG

Val Glu Arg Ser Gln Asn Gly Gly Glu Pro Asp Phe His Ala Val Glu Pro Tyr
GTG GAG CGG TCC CAG AAC GGA GGC GAA CCT GAC TTC CAT GCG GTT GAA CCC TAC

Thr Lys Lys Glu Leu Ser Ala Val Thr Phe Pro Asp Ile Ile Arg Asn Tyr Lys
ACG AAG AAA GAA CTT TCT GCT GTT ACT TTC CCT GAC ATC ATT CGC AAT TAC AAA

Val Met Ala Ala Glu Asn Ile Pro Glu Asn Pro Leu Lys Tyr Leu Tyr Pro Asn
GTC ATG GCT GCT GAG AAT ATT CCT GAG AAT CCC CTG AAG TAT CTG TAT CCA AAT
```

PCT/US93/07660

Figure 3B

```
Ile Asp Lys Asp His Ala Phe Gly Lys Tyr Tyr Ser Arg Pro Lys Glu Ala Pro
ATT GAC AAA GAC CAT GCC TTT GGA AAG TAT TAC TCC AGG CCA AAG GAA GCA CCA

Glu Pro Met Glu Leu Asp Gly Pro Lys Gly Thr Gly Tyr Ile Lys Thr Glu Leu
GAG CCA ATG GAA CTT GAT GGC CCT AAA GGA ACT GGA TAT ATC AAG ACT GAG TTG

Ile Ser Val Ser Glu Val
ATT TCT GTG TCT GAA GTG TAAGTGAACACAGAAGAGTGACATGTTTACAAACCTCAAGCCAGCCT

TGCTCCTGGCTGGGGCCTGTTGAAGATGCTTGTATTTTACTTTTCCATTGTAATTGCTATCGCCATCACAG

CTGAACTTGTTGAGATCCCCGTGTTACTGCCTATCAGCATTTTACTACTTTAAAAAAAAAAAAAAAAAGCCA

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TGAGCAAAAGTTGAA
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EP 0 729 754 A2

Figure 3C

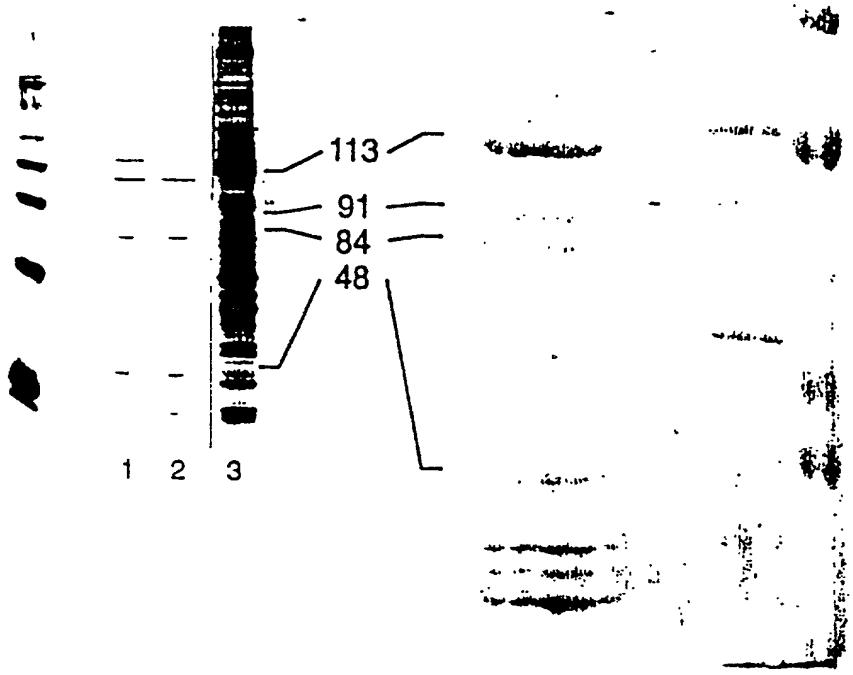
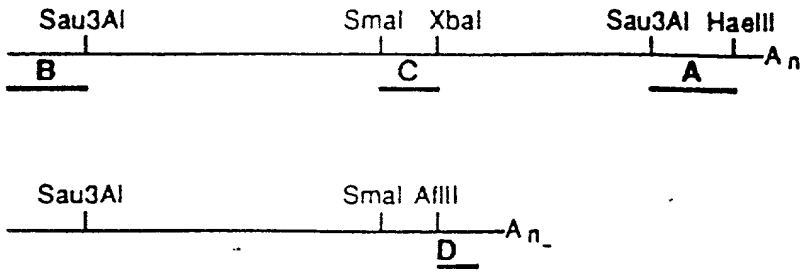


Figure 4


Sau3AI
SmaI
XbaI
Sau3AI
HaeIII
An
B
C
A
Sau3AI
SmaI
AflII
An
D

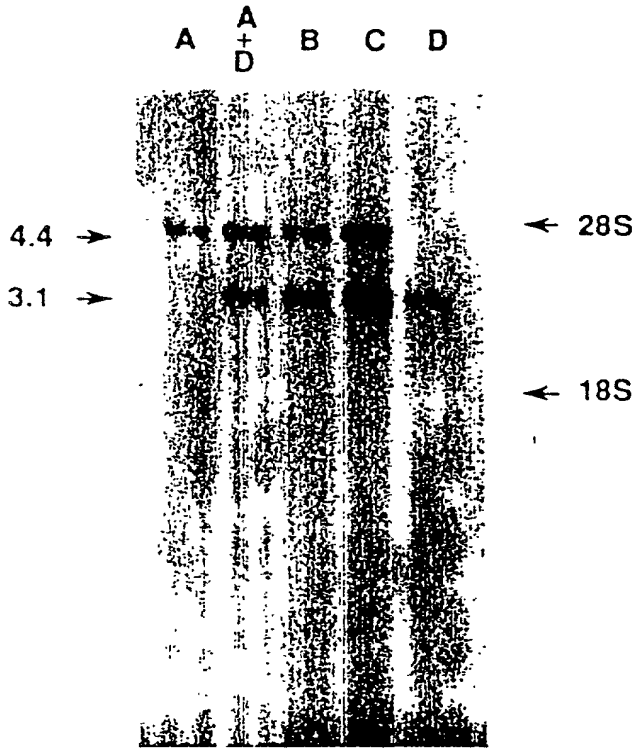

A
A + D
B
C
D
4.4
3.1
28S
18S

Figure 5

```
  1 MSQWYELQQLDSKFLEQVHQLYDDSFPMEIRQYLAQWLEKQDWEHAANDV
 51 SFATIRFHDLLSQLDDQYSRFSLENNFLLQHNIRKSKRNLQDNFQEDPIQ
101 MSHIIYSCLKEERKILENAQRFNQAQSGNIQSTVHILDKQKELDSKVRNVK
151 DKVMCIEHEIKSLEDLQDEYDFKCKTLQNREHETNGVAKSDQKQEQLLLK
201 KMYLMLDNKRKEVVHKIIELLNVTELTQNALINDELVEWKRRQQSACIGG
251 PPNACLDQLQQVRQQLKKLEELEQKYTYEHDPITKNKQVLWDRTFSLFQQ
301 LIQSSFVVERQPCMPTHPQRPLVLKTGVQFTVKLRLLVKLQELNYNLKVK
351 VLFDKDVNERNTVKGFRKFNILGTH[illegible]KVMNMEESTNGSLAAEFRHLQLKE
401 QKNAGTRTHEGPLIVTEELHSLSFETQLCQPGLVIDLETTSLPVVVISNV
451 SQLPSGWASILWYNMLVAEPRNLSFFLTPPCARWAQLSEVLSWQFSSVTK
                 127
501 RGLNYDQLIMMLGEKLLGPNASPDGLIPWTRFCKENINDKNFPFWLWIESI
                   119
551 LELIKKHLLPLWNDGCIMGFISKERERALLKDQQPGTFLLRFSESSREGA
601 ITFTWVERSQNGGEPDFHAVEPYTKKELSAVTFPDIIRNYKVMAAENIPE
                                                    113a
651 NPLKYLYPNIDKDHAFGKYYSRPKEAPEPMELDGPKGTGYIKTELISVSE
                 113b
701 VHPSRLQTTDNLLPMSPEEFDEVSRIVGSVEFDSMMNTV
    ▲
last amino acid of 84 kd
```

Figure 6

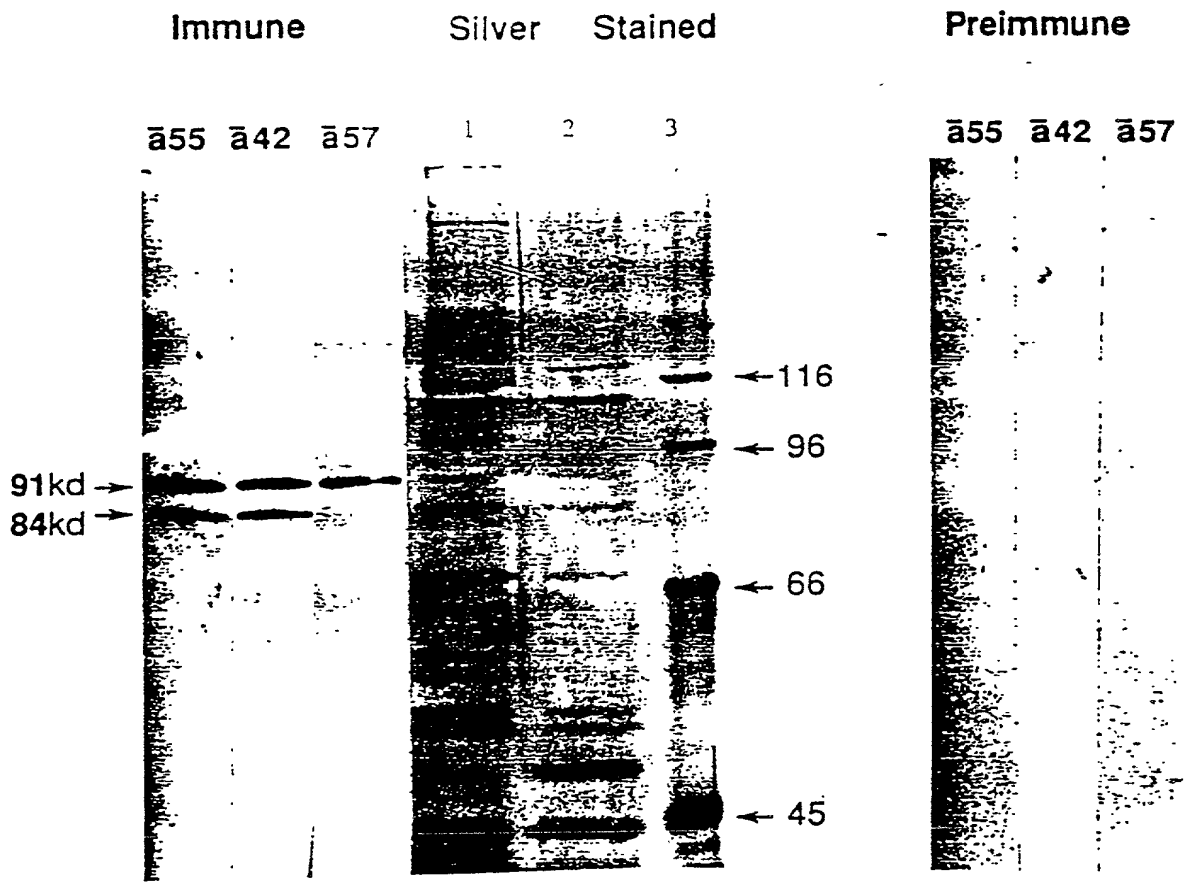
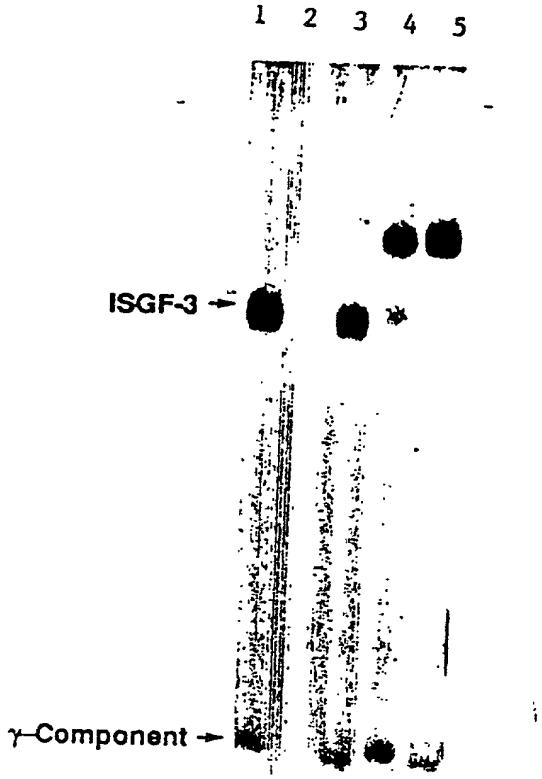
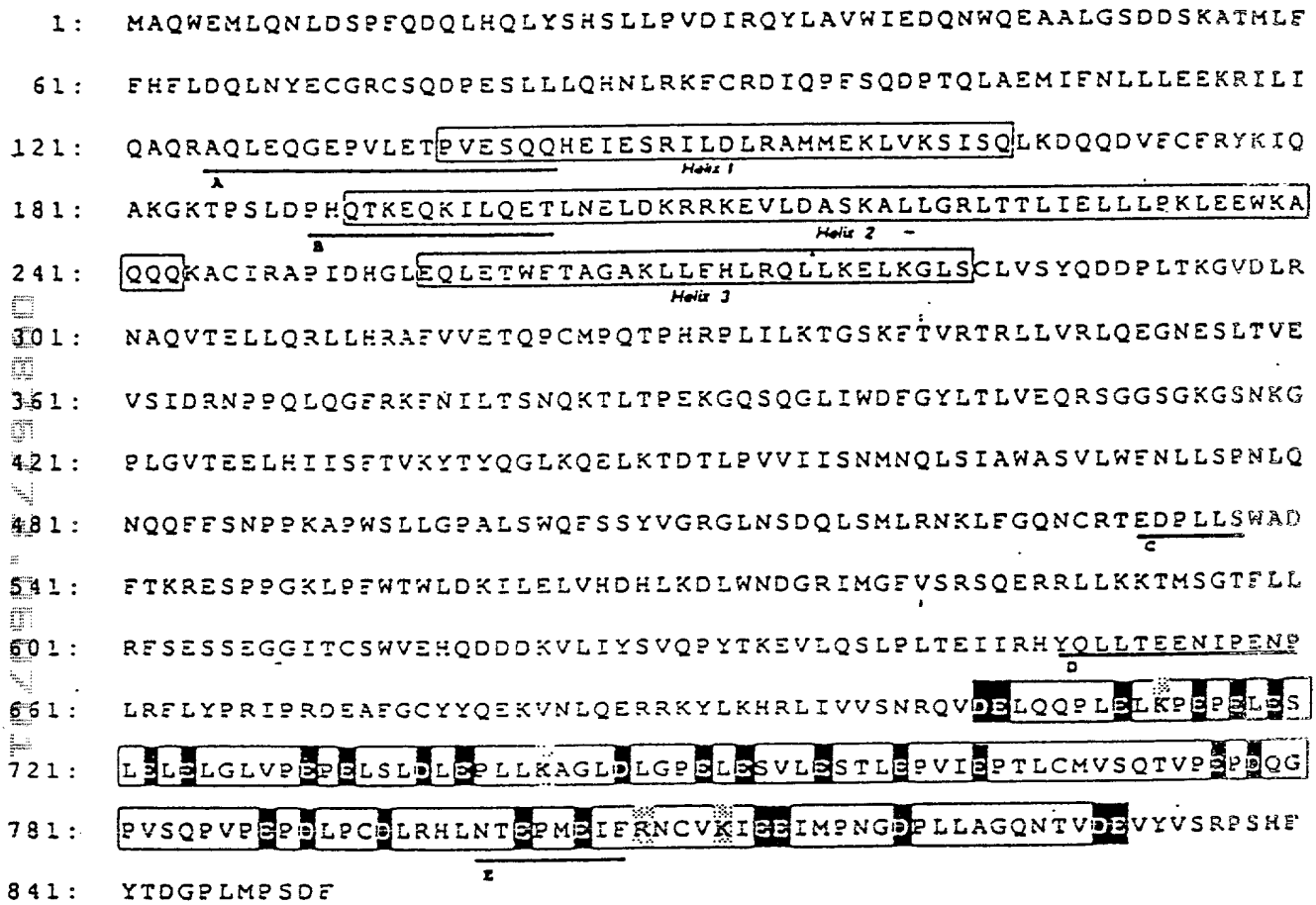

Immune
Silver Stained
Preimmune
ā55 ā42 ā57
1 2 3
ā55 ā42 ā57
91kd
84kd
116
96
66
45

Figure 7A



PCT/US90/07650

Figure 7B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121: QAQRAQLEQGEPVLETPVESQQHEIESRILDLRAMMEKLVKSISQLKDQQDVFCFRYKIQ
181: AKGKTPSLDPHQTKEQKILQETLNELDKRRKEVLDASKALLGRLTTLIELLLPKLEEWKA
241: QQQKACIRAPIDHGLEQLETWFTAGAKLLFHLRQLLKELKGLSCLVSYQDDPLTKGVDLR
301: NAQVTELLQRLLHRAFVVETQPCMPQTPHRPLILKTGSKFTVRTRLLVRLQEGNESLTVE
361: VSIDRNPPQLQGFRKFNILTSNQKTLTPEKGQSQGLIWDFGYLTLVEQRSGGSGKGSNKG
421: PLGVTEELHIISFTVKYTYQGLKQELKTDTLPVVIISNMNQLSIAWASVLWFNLLSPNLQ
481: NQQFFSNPPKAPWSLLGPALSWQFSSYVGRGLNSDQLSMLRNKLFGQNCRTEDPLLSWAD
541: FTKRESPPGKLPFWTWLDKILELVHDHLKDLWNDGRIMGFVSRSQERRLLKKTMSGTFLL
601: RFSESSEGGITCSWVEHQDDDKVLIYSVQPYTKEVLQSLPLTEIIRHYQLLTEENIPENP
661: LRFLYPRIPRDEAFGCYYQEKVNLQERRKYLKHRLIVVSNRQVDELQQPLELKPEPELES
721: LELELGLVPEPELSLDLEPLLKAGLDLGPELESVLESTLEPVIEPTLCMVSQTVPEPDQG
781: PVSQPVPEPPLPCDLRHLNTEPMEIFRNCVKIGEIMPNGDPLLAGQNTVDEVYVSRPSHF
841: YTDGPLMPSDF

Figure 8 A

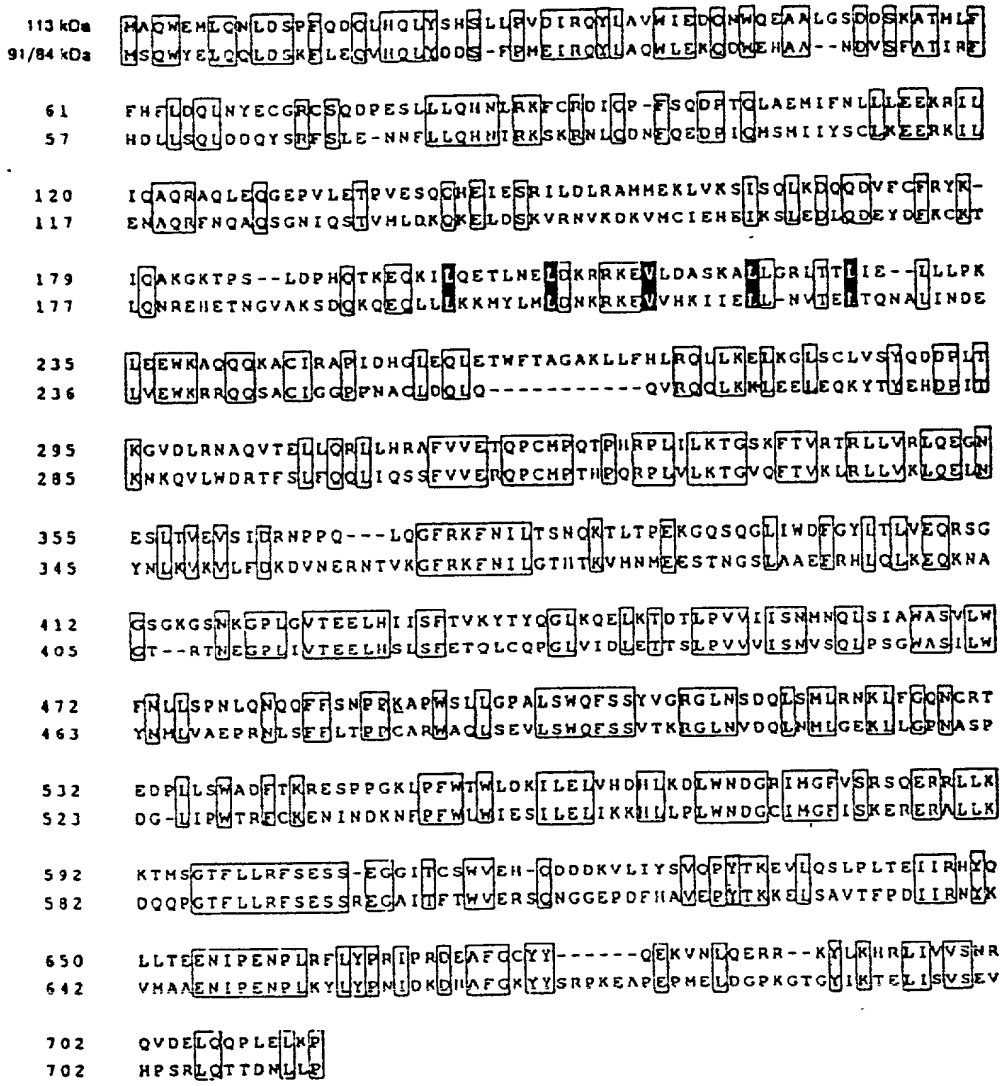

Figure 8B

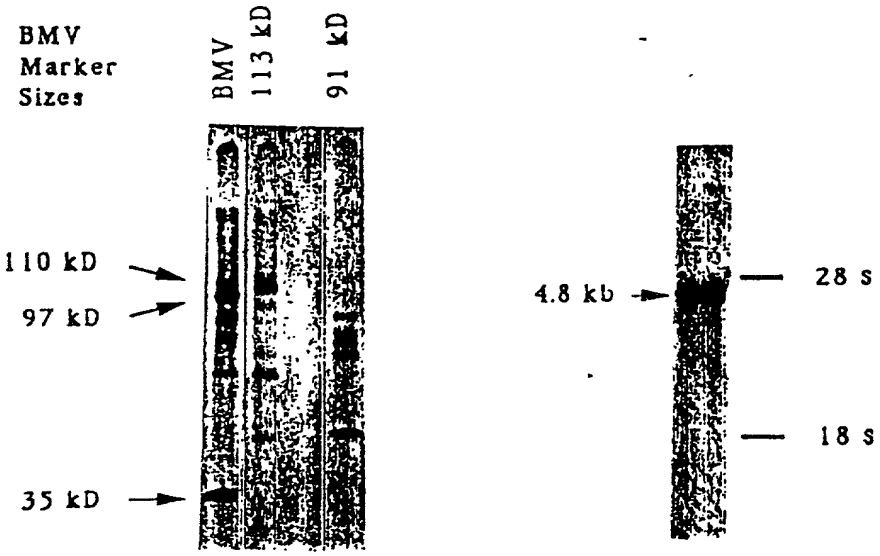

Figure 9

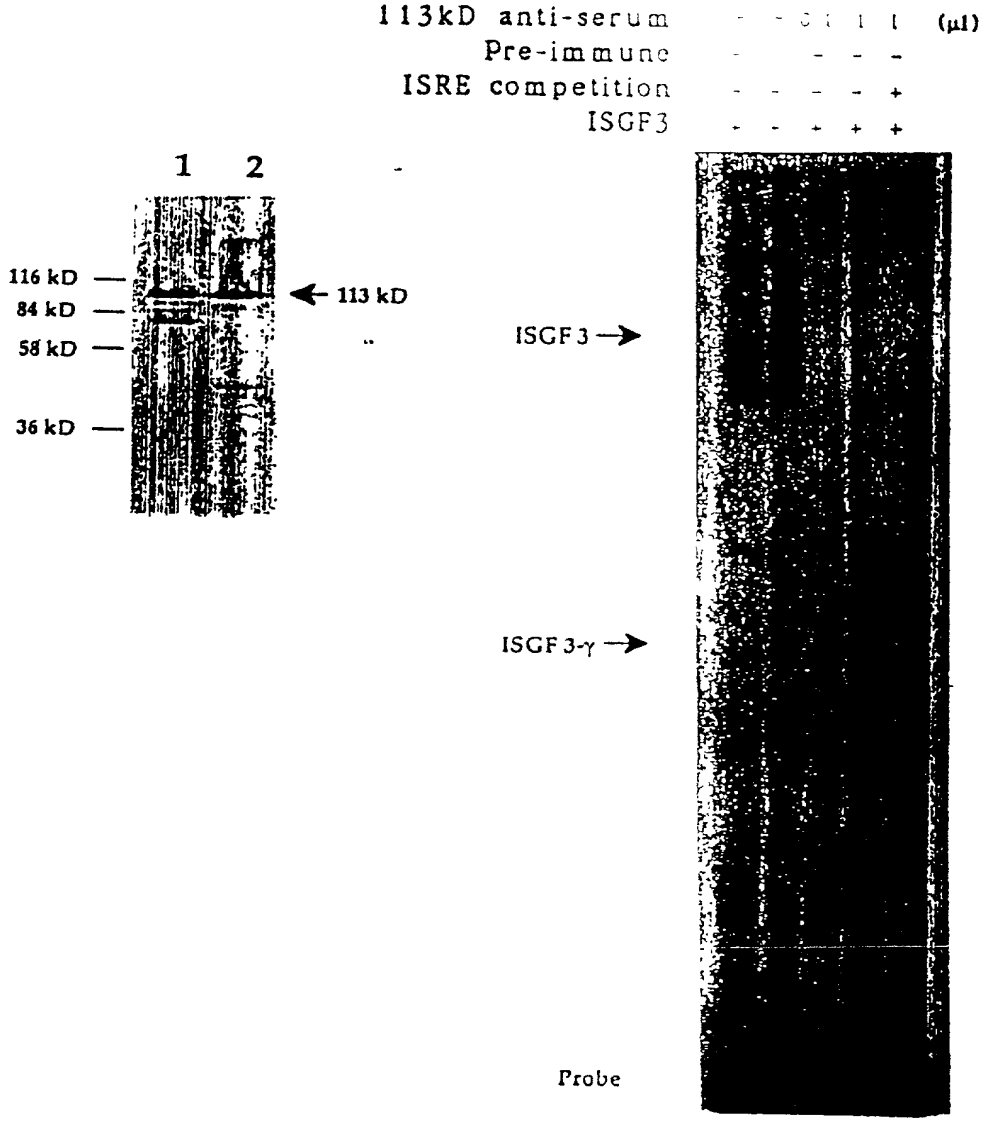
113kD anti-serum
Pre-immune
ISRE competition
ISGF3
(µl)
1
2
116 kD
84 kD
58 kD
36 kD
113 kD
ISGF3
ISGF3-γ
Probe

Figure 10

Figure 11

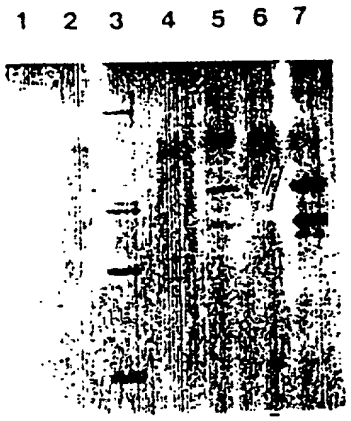

Figure 12

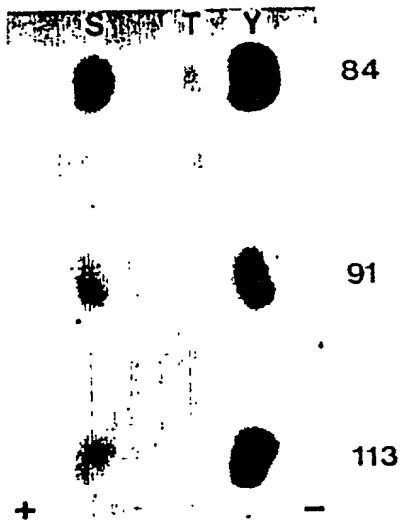

Figure 11, 12

1 MSQWFELQQL DSKFLEQVHQ LYDDSFPMEI RQYLAQWLEK QDWEHAAYDV

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101 MSMIIYNCLK EERKILENAQ RFNQAQEGNI QNTVMLDKQK ELDSKVRNVK

151 DQVMCIEQEI KTLEELQDEY DFKCKTSQNR EGEANGVAKS DQKQEQLLLH

201 KMFLMLDNKR KEIIHKIREL LNSIELTQNT LINDELVEWK RRQQSACIGG

251 PPNACLDQLQ TWFTIVAETL QQIRQQLKKL EELEQKFTYE PDPITKNKQV

301 LSDRTFLLFQ QLIQSSFVVE RQPCMPTHPQ RPLVLKTGVQ FTVKSRLLVK

351 LQESNLLTKV KCHFDKDVNE KNTVKGFRKF NILGTHTKVM NMEESTNGSL

401 AAELRHLQLK EQKNAGNRTN EGPLIVTEEL HSLSFETQLC QPGLVIDLET

451 TSLPVVVISN VSQLPSGWAS ILWYNMLVTE PRNLSFFLNP PCAWWSQLSE

501 VLSWQFSSVT KRGLNADQLS MLGEKLLGPN AGPDGLIPWT RFCKENINDK

551 NFSFWPWIDT ILELIKNDLL CLWNDGCIMG FISKERERAL LKDQQPGTFL

601 LRFSESSREG AITFTWVERS QNGGEPDFHA VEPYTKKELS AVTFPDIIRN

651 YKVMAAENIP ENPLKYLYPN IDKDHAFGKY YSRPKEAPEP MELDDPKRTG

701 YIKTELISVS EVHPSRLQTT DNLLPMSPEE FDEMSRIVGP EFDSMMSTV

Figure 13A

```
   1  caggatgtca cagtggttcg agcttcagca gctggactcc aagttcctgg
  51  agcaggtcca ccagctgtac gatgacagtt tccccatgga aatcagacag
 101  tacctggccc agtggctgga aaagcaagac tgggagcacg ctgcctatga
 151  tgtctcgttt gcgaccatcc gcttccatga cctcctctca cagctggacg
 201  accagtacag ccgcttttct ctggagaata atttcttgtt gcagcacaac
 251  atacggaaaa gcaagcgtaa tctccaggat aacttccaag aagatcccgt
 301  acagatgtcc atgatcatct acaactgtct gaaggaagaa aggaagattt
 351  tggaaaatgc ccaaagattt aatcaggccc aggagggaaa tattcagaac
 401  actgtgatgt tagataaaca gaaggagctg gacagtaaag tcagaaatgt
 451  gaaggatcaa gtcatgtgca tagagcagga aatcaagacc ctagaagaat
 501  tacaagatga atatgacttt aaatgcaaaa cctctcagaa cagagaaggt
 551  gaagccaatg gtgtggcgaa gagcgaccaa aaacaggaac agctgctgct
 601  ccacaagatg tttttaatgc ttgacaataa gagaaaggag ataattcaca
 651  aaatcagaga gttgctgaat tccatcgagc tcactcagaa cactctgatt
 701  aatgacgagc tcgtggagtg gaagcgaagg cagcagagcg cctgcatcgg
 751  gggaccgccc aacgcctgcc tggatcagct gcaaacgtgg ttcaccattg
 801  ttgcagagac cctgcagcag atccgtcagc agcttaaaaa gctggaggag
 851  ttggaacaga aattcaccta tgagcccgac cctattacaa aaaacaagca
 901  ggtgttgtca gatcgaacct tcctcctctt ccagcagctc attcagagct
 951  ccttcgtggt agaacgacag ccgtgcatgc ccactcaccc gcagaggccc
1001  ctggtcttga agactggggt acagttcact gtcaagtcga gactgttggt
1051  gaaattgcaa gagtcgaatc tattaacgaa agtgaaatgt cactttgaca
1101  aagatgtgaa cgagaaaaac acagttaaag gatttcggaa gttcaacatc
1151  ttgggtacgc acacaaaagt gatgaacatg gaagaatcca ccaacggaag
1201  tctggcagct gagctccgac acctgcaact gaaggaacag aaaaacgctg
1251  ggaacagaac taatgagggg cctctcattg tcaccgaaga acttcactct
1301  cttagctttg aaacccagtt gtgccagcca ggcttggtga ttgacctgga
1351  gaccacctct cttcctgtcg tggtgatctc caacgtcagc cagctcccca
```

Figure 13B

```
1401  gtggctgggc gtctatcctg tggtacaaca tgctggtgac agagcccagg
1451  aatctctcct tcttcctgaa ccccccgtgc gcgtggtggt cccagctctc
1501  agaggtgttg agttggcagt tttcatcagt caccaagaga ggtctgaacg
1551  cagaccagct gagcatgctg ggagagaagc tgctgggccc taatgctggc
1601  cctgatggtc ttattccatg gacaaggttt tgtaaggaaa atattaatga
1651  taaaaatttc tccttctggc cttggattga caccatccta gagctcatta
1701  agaacgacct gctgtgcctc tggaatgatg ggtgcattat gggcttcatc
1751  agcaaggagc gagaacgcgc tctgctcaag gaccagcagc cagggacgtt
1801  cctgcttaga ttcagtgaga gctcccggga aggggccatc acattcacat
1851  gggtggaacg gtcccagaac ggaggtgaac ctgacttcca tgccgtggag
1901  ccctacacga aaaaagaact ttcagctgtt actttcccag atattattcg
1951  caactacaaa gtcatggctg ccgagaacat accagagaat cccctgaagt
2001  atctgtaccc caatattgac aaagaccacg cctttgggaa gtattattcc
2051  agaccaaagg aagcaccaga accgatggag cttgacgacc ctaagcgaac
2101  tggatacatc aagactgagt tgatttctgt gtctgaagtc caccttcta
2151  gacttcagac cacagacaac ctgcttccca tgtctccaga ggagtttgat
2201  gagatgtccc ggatagtggg ccccgaattt gacagtatga tgagcacagt
2251  ataaacacga atttctctct ggcgaca
```

Figure 13C

```
   1  MSQWNQVQQL EIKFLEQVDQ FYDDNFPMEI RHLLAQWIET QDWEVASNNE

  51  TMATILLQNL LIQLDEQLGR VSKEKNLLLI HNLKRIRKVL QGKFHGNPMH

 101  VAVVISNCLR EERRILAAAN MPIQGPLEKS LQSSSVSERQ RNVEHKVSAI

 151  KNSVQMTEQD TKYLEDLQDE FDYRYKTIQT MDQGDKNSIL VNQEVLTLLQ

 201  EMLNSLDFKR KEALSKMTQI VNETDLLMNS MLLEELQDWK KRHRIACIGG

 251  PLHNGLDQLQ NCFTLLAESL FQLRQQLEKL QEQSTKMTYE GDPIPAQRAH

 301  LLERATFLIY NLFKNSFVVE RHACMPTHPQ RPMVLKTLIQ FTVKLRLLIK

 351  LPELNYQVKV KASIDKNVST LSNRRFVLCG THVKAMSSEE SSNGSLSVEL

 401  DIATQGDEVQ YWSKGNEGCH MVTEELHSIT FETQICLYGL TINLETSSLP

 451  VVMISNVSQL PNAWASIIWY NVSTNDSQNL VFFNNPPSVT LGQLLEVMSW

 501  QFSSYVGRGL NSEQLNMLAE KLTVQSNYND GHLTWAKFCK EHLPGKTFTF

 551  WTWLEAILDL IKKHILPLWI DGYIMGFVSK EKERLLLKDK MPGTFLLRFS

 601  ESHLGGITFT WVDQSENGEV RFHSVEPYNK GRLSALAFAD ILRDYKVIMA

 651  ENIPENPLKY LYPDIPKDKA FGKHYSSQPC EVSRPTERGD KGYVPSVFIP

 701  ISTIRSDSTE PQSPSDLLPM SPSAYAVLRE NLSPTTIETA MNSPYSAE
```

Figure 14A

```
  1  tgccactacc tggacggaga gagagagagc agcatgtctc agtggaatca
 51  agtccaacaa ttagaaatca agtttttgga gcaagtagat cagttctatg
101  atgacaactt tcctatggaa atccggcatc tgctagctca gtggattgag
151  actcaagact gggaagtagc ttctaacaat gaaactatgg caacaattct
201  gcttcaaaac ttactaatac aattggatga acagttgggg cgggtttcca
251  aagaaaaaaa tctgctattg attcacaatc taaagagaat tagaaaagtt
301  cttcagggca agtttcatgg aaatccaatg catgtagctg tggtaatttc
351  aaattgctta agggaagaga ggagaatatt ggctgcagcc aacatgccta
401  tccagggacc tctggagaaa tccttacaga gttcttcagt ttctgaaaga
451  caaaggaatg tggaacacaa agtgtctgcc attaaaaaca gtgtgcagat
501  gacagaacaa gataccaaat acttagaaga cctgcaagat gagtttgact
551  acaggtataa aacaattcag acaatggatc agggtgacaa aaacagtatc
601  ctggtgaacc aggaagtttt gacactgctg caagaaatgc ttaatagtct
651  ggacttcaag agaaaggaag cactcagtaa gatgacgcag atagtgaacg
701  agacagacct gctcatgaac agcatgcttc tagaagagct gcaggactgg
751  aaaaagcggc acaggattgc ctgcattggt ggcccgctcc acaatgggct
801  ggaccagctt cagaactgct ttaccctact ggcagagagt cttttccaac
851  tcagacagca actggagaaa ctacaggagc aatctactaa aatgacctat
```

Figure 14B

901 gaaggggatc ccatcccctgc tcaaagagca cacctcctgg aaagagctac

951 cttcctgatc tacaaccttt tcaagaactc atttgtggtc gagcgacacg

1001 catgcatgcc aacgcacccct cagaggccga tggtacttaa aaccctcatt

1051 cagttcactg taaaactgag attactaata aaattgccgg aactaaacta

1101 tcaggtgaaa gtaaaggcgt ccattgacaa gaatgtttca actctaagca

1151 atagaagatt tgtgctttgt ggaactcacg tcaaagctat gtccagtgag

1201 gaatcttcca atgggagcct ctcagtggag ttagacattg caacccaagg

1251 agatgaagtg cagtactgga gtaaaggaaa cgagggctgc cacatggtga

1301 cagaggagtt gcattccata acctttgaga cccagatctg cctctatggc

1351 ctcaccatta acctagagac cagctcatta cctgtcgtga tgatttctaa

1401 tgtcagccaa ctacctaatg catgggcatc catcatttgg tacaatgtat

1451 caactaacga ctcccagaac ttggttttct ttaataaccc tccatctgtc

1501 actttgggcc aactcctgga agtgatgagc tggcaatttt catcctatgt

1551 cggtcgtggc cttaattcag agcagctcaa catgctggca gagaagctca

1601 cagttcagtc taactacaat gatggtcacc tcacctgggc caagttctgc

1651 aaggaacatt tgcctggcaa aacatttacc ttctggactt ggcttgaagc

1701 aatattggac ctaattaaaa aacatattct tcccctctgg attgatgggt

1751 acatcatggg atttgttagt aaagagaagg aacggcttct gctcaaagat

1801 aaaatgcctg ggacattttt gttaagattc agtgagagcc atcttggagg

Figure 14C

```
1851  gataaccttc acctgggtgg accaatctga aaatggagaa gtgagattcc

1901  actctgtaga accctacaac aaagggagac tgtcggctct ggccttcgct

1951  gacatcctgc gagactacaa ggttatcatg gctgaaaaca tccctgaaaa

2001  ccctctgaag tacctctacc ctgacattcc caaagacaaa gcctttggca

2051  aacactacag ctcccagccg tgcgaagtct caagaccaac cgaacgggga

2101  gacaagggtt acgtcccctc tgtttttatc cccatttcaa caatccgaag

2151  cgattccacg gagccacaat ctccttcaga ccttctcccc atgtctccaa

2201  gtgcatatgc tgtgctgaga gaaaacctga gcccaacgac aattgaaact

2251  gcaatgaatt ccccatattc tgctgaatga cggtgcaaac ggacacttta

2301  aagaaggaag cagatgaaac tggagagtgt tcttaccat agatcacaat

2351  ttatttcttc ggctttgtaa atacc
```

Figure 14D

```
  1  MAQWNQLQQL DTRYLKQLHQ LYSDTFPMEL RQFLAPWIES QDWAYAASKE
 51  SHATLVFHNL LGEIDQQYSR FLQESNVLYQ HNLRRIKQFL QSRYLEKPME
101  IARIVARCLW EESRLLQTAA TAAQQGGQAN HPTAAVVTEK QQMLEQHLQD
151  VRKRVQDLEQ KMKVVENLQD DFDFNYKTLK SQGDMQDLNG NNQSVTRQKM
201  QQLEQMLTAL DQMRRSIVSE LAGLLSAMEY VQKTLTDEEL ADWKRRPEIA
251  CIGGPPNICL DRLENWITSL AESQLQTRQQ IKKLEELQQK VSYKGDPIVQ
301  HRPMLEERIV ELFRNLMKSA FVVERQPCMP MHPDRPLVIK TGVQFTTKVR
351  LLVKFPELNY QLKIKVCIDK DSGDVAALRG SRKFNILGTN TKVMNMEESN
401  NGSLSAEFKH LTLREQRCGN GGRANCDASL IVTEELHLIT FETEVYHQGL
451  KIDLETHSLP VVVISNICQM PNAWASILWY NMLTNNPKNV NFFTKPPIGT
501  WDQVAEVLSW QFSSTTKRGL SIEQLTTLAE KLLGPGVNYS GCQITWAKFC
551  KENMAGKGFS FWVWLDNIID LVKKYILALW NEGYIMGFIS KERERAILST
601  KPPGTFLLRF SESSKEGGVT FTWVEKDISG KTQIQSVEPY TKQQLNNMSF
651  AEIIMGYKIM DATNILVSPL VYLYPDIPKE EAFGKYCRPE SQEHPEADPG
701  SAAPYLKTKF ICVTPTTCSN TIDLPMSPRT LDSLMQFGNN GEGAEPSAGG
751  QFESLTFDMD LTSECATSPM
```

Figure 15A

```
  1  gccgcgacca gccaggccgg ccagtcgggc tcagcccgga gacagtcgag

 51  acccctgact gcagcaggat ggctcagtgg aaccagctgc agcagctgga

101  cacacgctac ctgaagcagc tgcaccagct gtacagcgac acgttcccca

151  tggagctgcg gcagttcctg gcaccttgga ttgagagtca agactgggca

201  tatgcagcca gcaaagagtc acatgccacg ttggtgtttc ataatctctt

251  gggtgaaatt gaccagcaat atagccgatt cctgcaagag tccaatgtcc

301  tctatcagca caaccttcga agaatcaagc agtttctgca gagcaggtat

351  cttgagaagc caatggaaat tgcccggatc gtggcccgat gcctgtggga

401  agagtctcgc ctcctccaga cggcagccac ggcagcccag caaggggcc

451  aggccaacca cccaacagcc gccgtagtga cagagaagca gcagatgttg

501  gagcagcatc ttcaggatgt ccggaagcga gtgcaggatc tagaacagaa

551  aatgaaggtg gtggagaacc tccaggacga ctttgatttc aactacaaaa

601  ccctcaagag ccaaggagac atgcaggatc tgaatggaaa caaccagtct

651  gtgaccagac agaagatgca gcagctggaa cagatgctca cagccctgga

701  ccagatgcgg agaagcattg tgagtgagct ggcggggctc ttgtcagcaa

751  tggagtacgt gcagaagaca ctgactgatg aagagctggc tgactggaag

801  aggcggccag agatcgcgtg catcggaggc cctcccaaca tctgcctgga

851  ccgtctggaa aactggataa cttcattagc agaatctcaa cttcagaccc
```

Figure 15B

```
 901  gccaacaaat taagaaactg gaggagctgc agcagaaagt gtcctacaag
 951  ggcgacccta tcgtgcagca ccggcccatg ctggaggaga ggatcgtgga
1001  gctgttcaga aacttaatga agagtgcctt cgtggtggag cggcagccct
1051  gcatgcccat gcacccggac cggcccttag tcatcaagac tggtgtccag
1101  tttaccacga aagtcaggtt gctggtcaaa tttcctgagt tgaattatca
1151  gcttaaaatt aaagtgtgca ttgataaaga ctctggggat gttgctgccc
1201  tcagagggtc tcggaaattt aacattctgg gcacgaacac aaaagtgatg
1251  aacatggagg agtctaacaa cggcagcctg tctgcagagt tcaagcacct
1301  gacccttagg gagcagagat gtgggaatgg aggccgtgcc aattgtgatg
1351  cctccttgat cgtgactgag gagctgcacc tgatcacctt cgagactgag
1401  gtgtaccacc aaggcctcaa gattgaccta gagacccact ccttgccagt
1451  tgtggtgatc tccaacatct gtcagatgcc aaatgcttgg gcatcaatcc
1501  tgtggtataa catgctgacc aataacccca agaacgtgaa cttcttcact
1551  aagccgccaa ttggaacctg ggaccaagtg gccgaggtgc tcagctggca
1601  gttctcgtcc accaccaagc gagggctgag catcgagcag ctgacaacgc
1651  tggctgagaa gctcctaggg cctggtgtga actactcagg gtgtcagatc
1701  acatgggcta aattctgcaa agaaaacatg gctggcaagg gctactcctt
1751  ctgggtctgg ctagacaata tcatcgacct tgtgaaaaag tatatcttgg
1801  ccctttggaa tgaagggtac atcatgggtt tcatcagcaa ggagcgggag
```

Figure 15C

1851 cgggccatcc taagcacaaa gccccgggc accttcctac tgcgcttcag

1901 cgagagcagc aaagaaggag gggtcacttt cacttgggtg gaaaaggaca

1951 tcagtggcaa gacccagatc cagtctgtag agccatacac caagcagcag

2001 ctgaacaaca tgtcatttgc tgaaatcatc atgggctata agatcatgga

2051 tgcgaccaac atcctggtgt ctccacttgt ctacctctac cccgacattc

2101 ccaaggagga ggcatttgga aagtactgta ggcccgagag ccaggagcac

2151 cccgaagccg acccaggtag tgctgccccg tacctgaaga ccaagttcat

2201 ctgtgtgaca ccaacgacct gcagcaatac cattgacctg ccgatgtccc

2251 cccgcacttt agattcattg atgcagtttg gaaataacgg tgaaggtgct

2301 gagccctcag caggagggca gtttgagtcg ctcacgtttg acatggatct

2351 gacctcggag tgtgctacct cccccatgtg aggagctgaa accagaagct

2401 gcagagacgt gacttgagac acctgccccg tgctccaccc ctaagcagcc

2451 gaaccccata tcgtctgaaa ctcctaactt tgtggttcca gatttttttt

2501 tttaatttcc tacttctgct atctttgggc aatctgggca ctttttaaaa

2551 gagagaaatg agtgagtgtg ggtgataaac tgttatgtaa agaggagaga

2601 cctctgagtc tggggatggg gctgagagca gaagggaggc aaaggggaac

2651 acctcctgtc ctgcccgcct gccctccttt ttcagcagct cgggggttgg

2701 ttgttagaca agtgcctcct ggtgcccatg gctacctgtt gccccactct

2751 gtgagctgat accccattct gggaactcct ggctctgcac tttcaacctt

Figure 15D

```
2801  gctaatatcc acatagaagc taggactaag cccaggaggt tcctctttaa

2851  attaaaaaaa aaaaaaaaa
```

PCT/US00/27350

Figure 15E

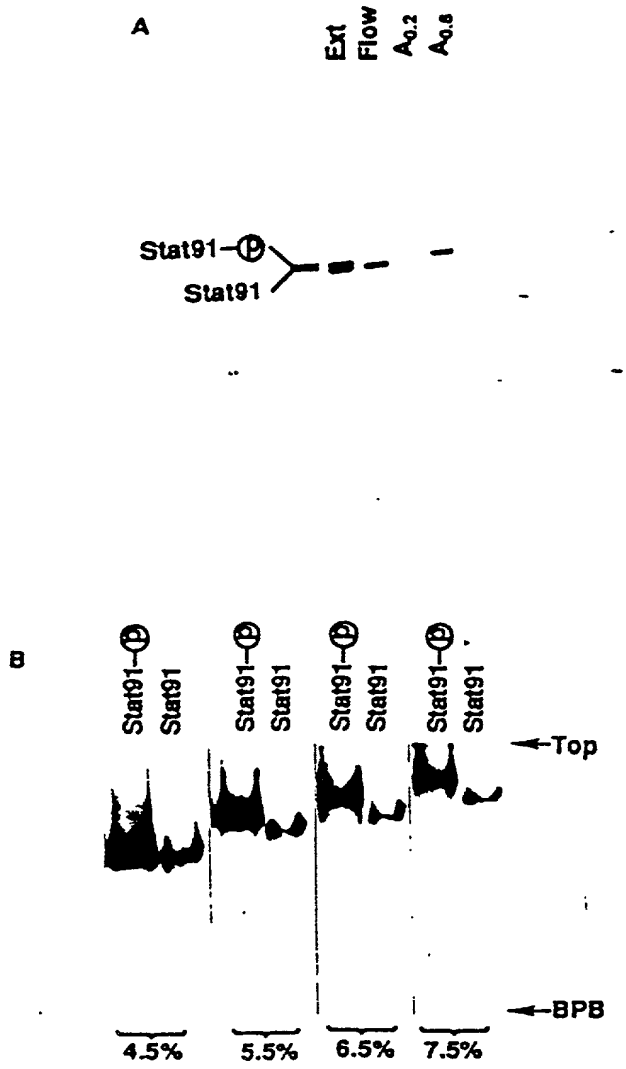

A
Ext
Flow
$A_{0.2}$
$A_{0.8}$
Stat91-P
Stat91
B
Stat91-P
Stat91
Top
BPB
4.5%
5.5%
6.5%
7.5%

Figure 16A, B

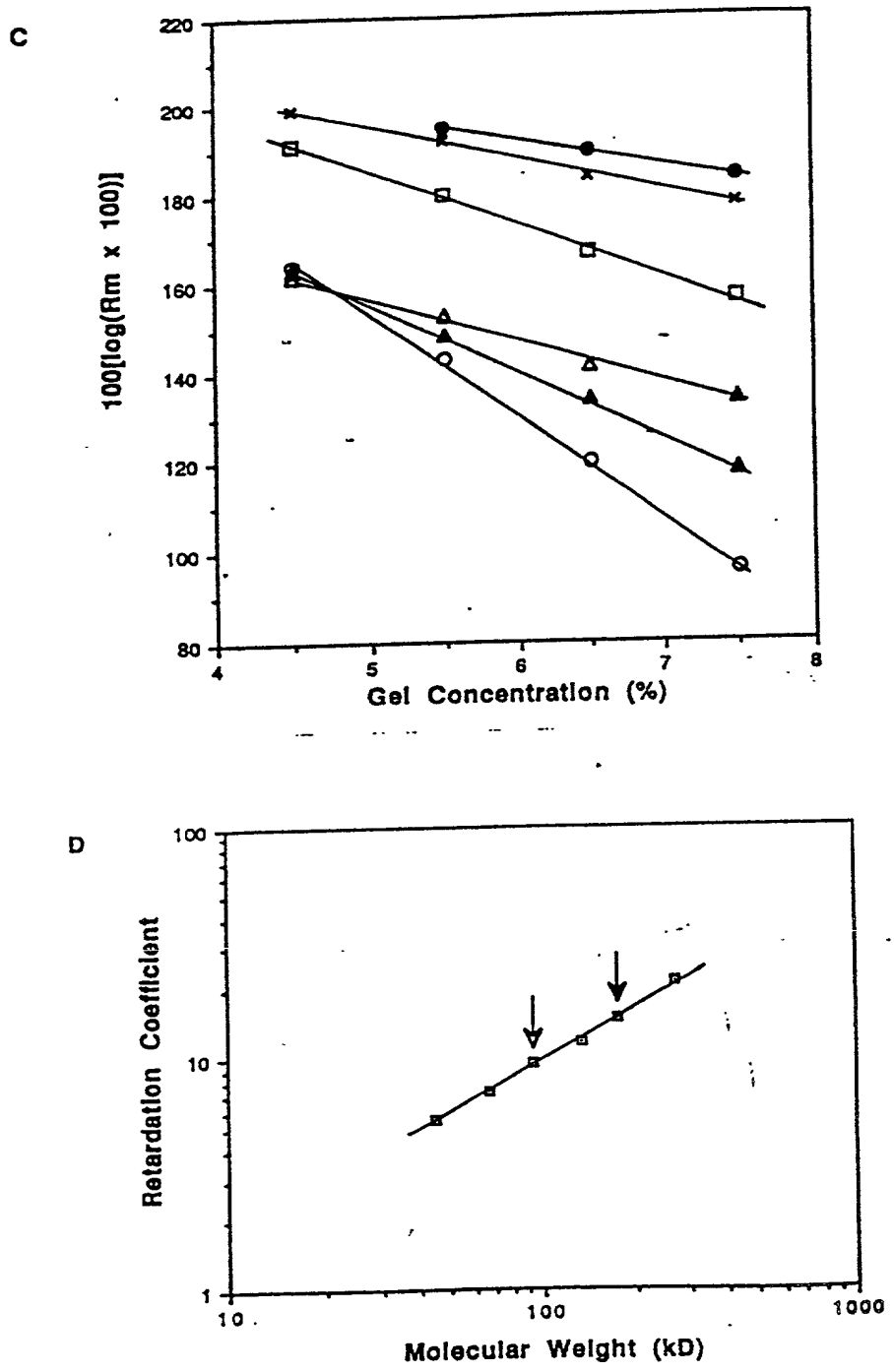

C
100[log(Rm x 100)]
220
200
180
160
140
120
100
80
4
5
6
7
8
Gel Concentration (%)
D
Retardation Coefficient
100
10
1
10
100
1000
Molecular Weight (kD)

Figure 16C,D

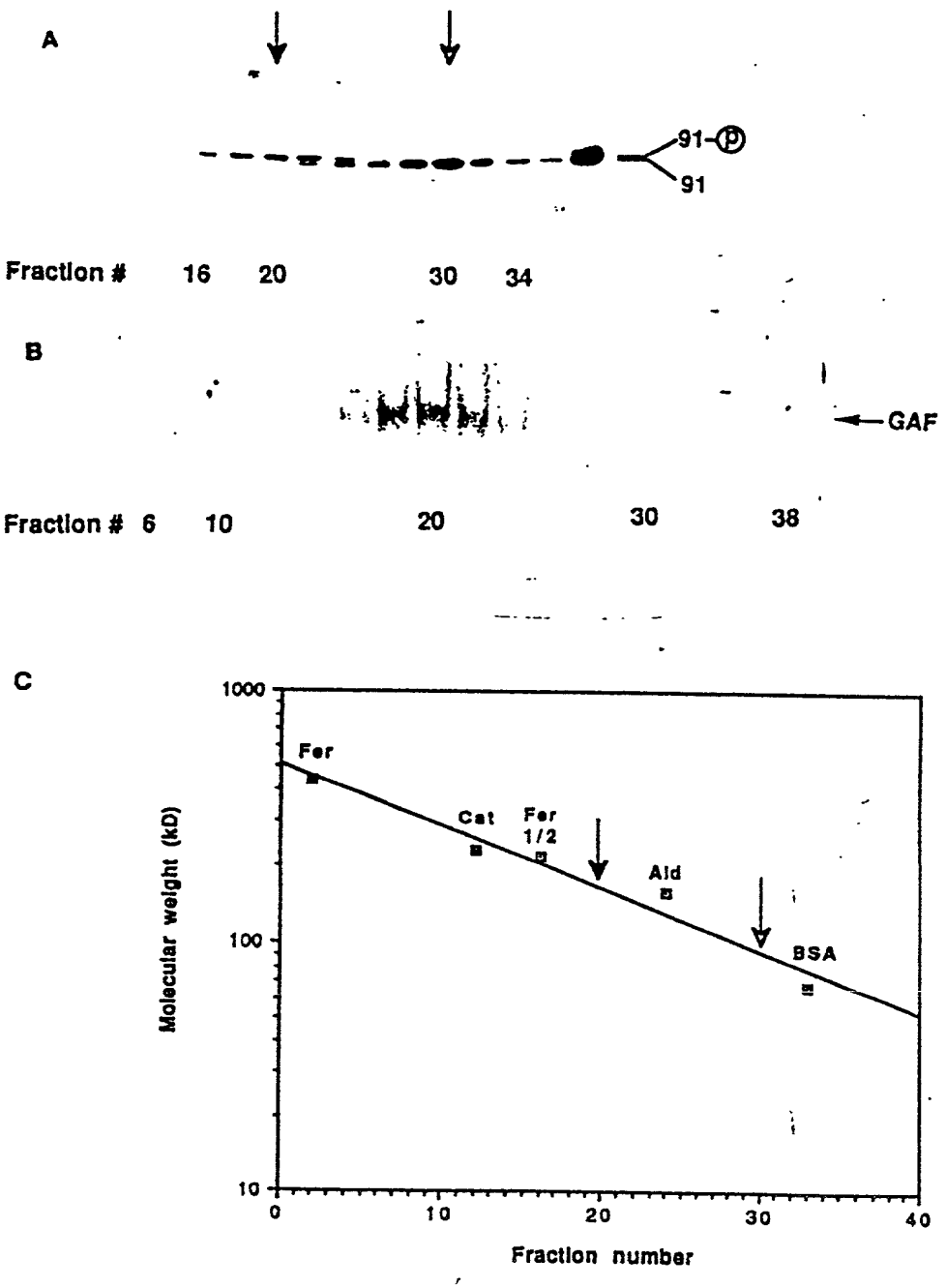

A
91-Ⓟ
91
Fraction # 16 20 30 34
B
GAF
Fraction # 6 10 20 30 38
C
1000
100
10
Molecular weight (kD)
Fer
Cat
Fer 1/2
Ald
BSA
0 10 20 30 40
Fraction number

Figure 17

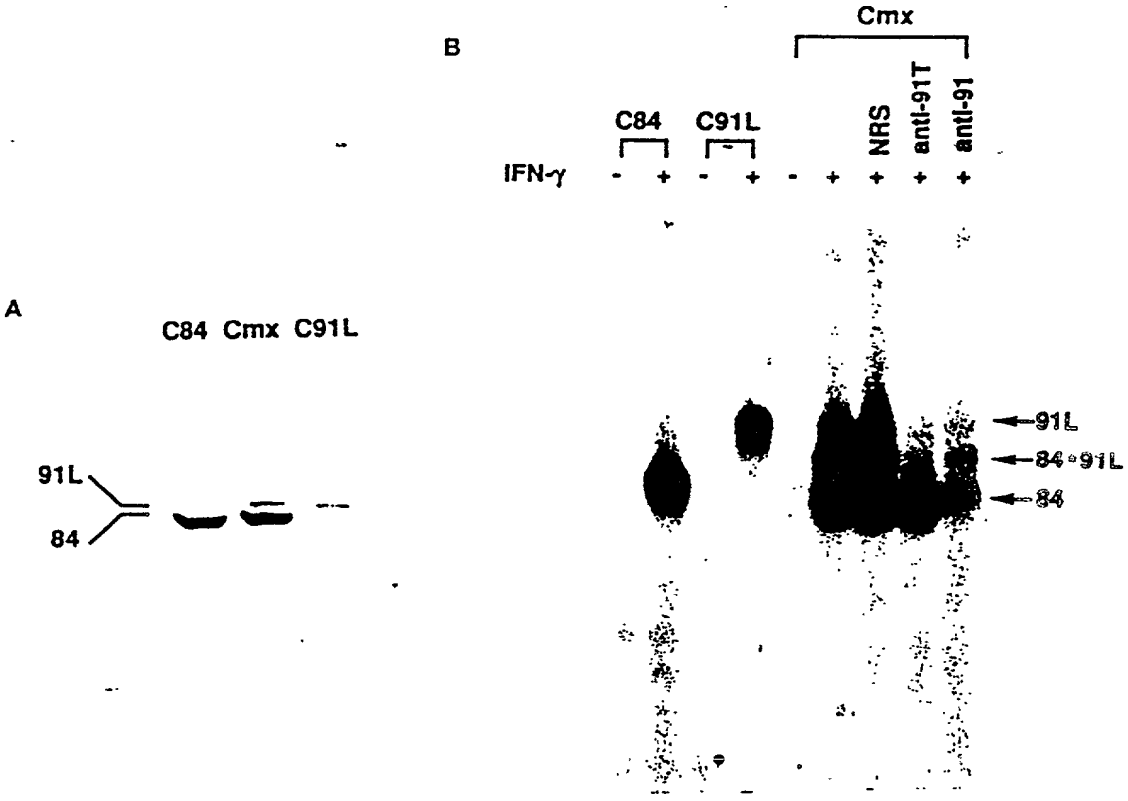

A
C84 Cmx C91L
91L
84
B
Cmx
C84
C91L
NRS
anti-91T
anti-91
IFN-γ
- + - + - + + + +
91L
84•91L
84

Figure 18

Figure 19

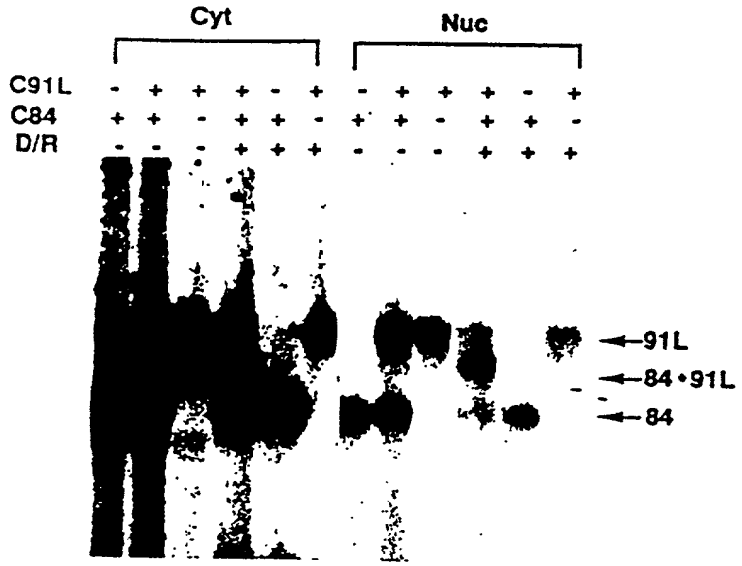


Figure 20

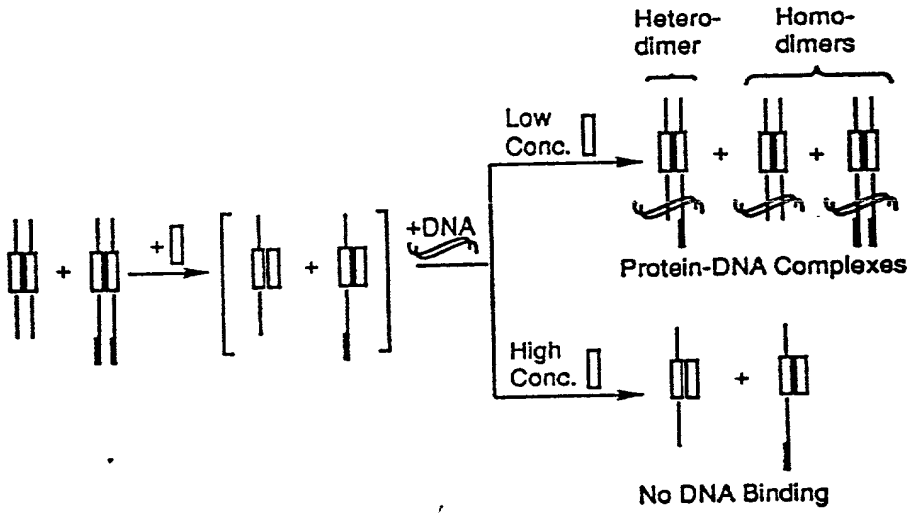


Figure 19, 20

EP 0 659 768 A2

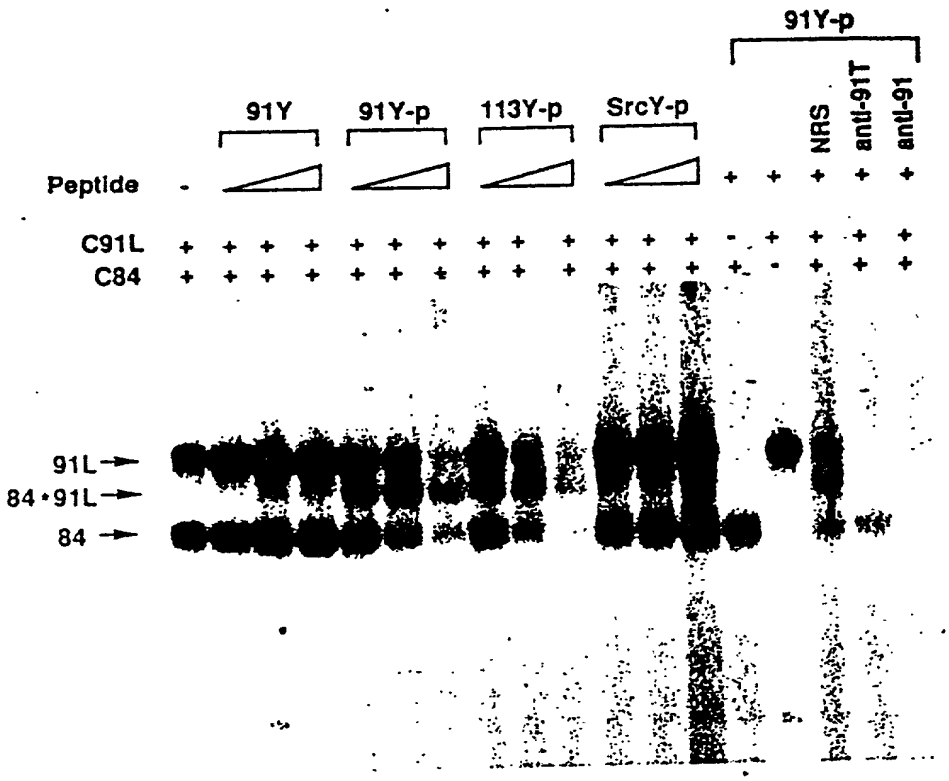
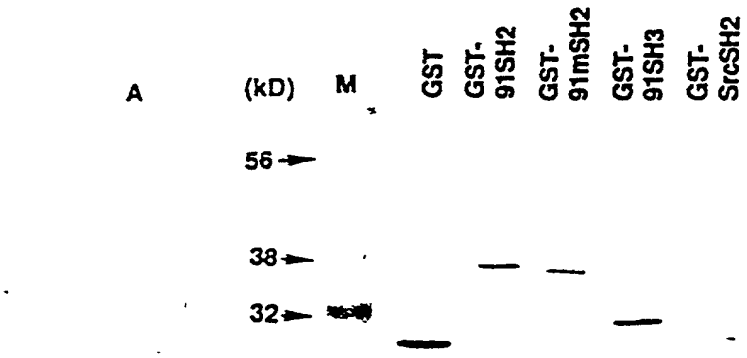

91Y-p
91Y
91Y-p
113Y-p
SrcY-p
NRS
anti-91T
anti-91
Peptide
C91L
C84
91L
84•91L
84

Figure 21


A
(kD)
M
GST
GST-91SH2
GST-91mSH2
GST-91SH3
GST-SrcSH2
56
38
32

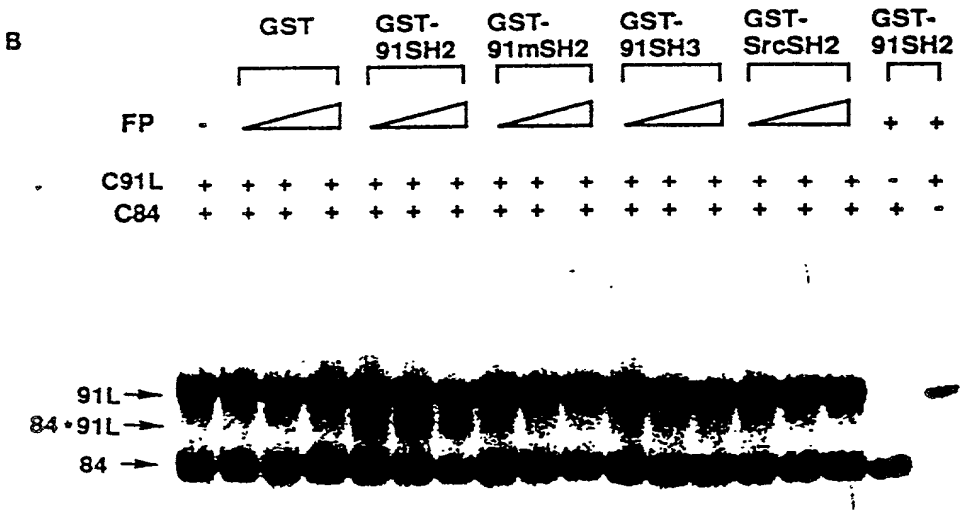

B
GST
GST-91SH2
GST-91mSH2
GST-91SH3
GST-SrcSH2
GST-91SH2
FP
C91L
C84
91L
84•91L
84

Figure 22

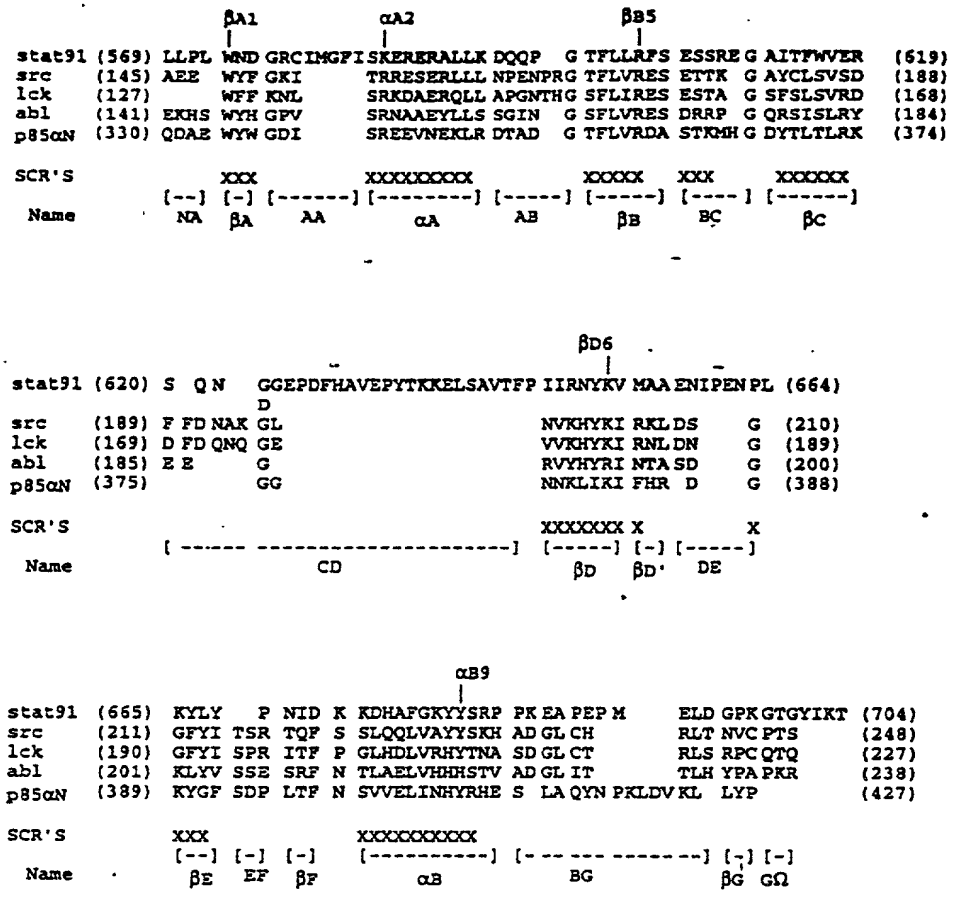

βA1
αA2
βB5
stat91 (569) LLPL WND GRCIMGFISKERERALLK DQQP G TFLLRFS ESSRE G AITFWVER (619)
src (145) AEE WYF GKI TRRESERLLL NPENPRG TFLVRES ETTK G AYCLSVSD (188)
lck (127) WFF KNL SRKDAERQLL APGNTHG SFLIRES ESTA G SFSLSVRD (168)
abl (141) EKHS WYH GPV SRNAAEYLLS SGIN G SFLVRES DRRP G QRSISLRY (184)
p85αN (330) QDAE WYW GDI SREEVNEKLR DTAD G TFLVRDA STKMH G DYTLTLRK (374)
SCR'S XXX XXXXXXXXX XXXXX XXX XXXXXX
[--] [-] [------] [--------] [-----] [-----] [----] [------]
Name NA βA AA αA AB βB BC βC
βD6
stat91 (620) S Q N GGEPDFHAVEPYTKKELSAVTFP IIRNYKV MAA ENIPEN PL (664)
D
src (189) F FD NAK GL NVKHYKI RKL DS G (210)
lck (169) D FD QNQ GE VVKHYKI RNL DN G (189)
abl (185) E E G RVYHYRI NTA SD G (200)
p85αN (375) GG NNKLIKI FHR D G (388)
SCR'S XXXXXXX X X
[------ ----------] [-----] [-] [-----]
Name CD βD βD' DE
αB9
stat91 (665) KYLY P NID K KDHAFGKYYSRP PK EA PEP M ELD GPK GTGYIKT (704)
src (211) GFYI TSR TQF S SLQQLVAYYSKH AD GL CH RLT NVC PTS (248)
lck (190) GFYI SPR ITF P GLHDLVRHYTNA SD GL CT RLS RPC QTQ (227)
abl (201) KLYV SSE SRF N TLAELVHHHSTV AD GL IT TLH YPA PKR (238)
p85αN (389) KYGF SDP LTF N SVVELINHYRHE S LA QYN PKLDV KL LYP (427)
SCR'S XXX XXXXXXXXXX
[--] [-] [-] [----------] [- -- --- --------] [-] [-]
Name βE EF βF αB BG βG GΩ

Figure 23